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**CARBON AND GRAPHITE FIBERS TO
CHLOROCARBONS AND CHLOROHYDROCARBONS**

CONTENT INDEX (vol 5)

(with hyperlinks)

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CARBON AND GRAPHITE FIBERS

Carbon fibers are the primary reinforcement used to increase the stiffness and strength of lightweight advanced composites commonly used in aerospace, recreation, and industrial applications. The term carbon fiber generally refers to a variety of filamentary products composed of more than 90% carbon, 5–10 μm in filament diameter, produced via the pyrolysis of polyacrylonitrile (PAN), pitch, or rayon. Carbon fibers are often referred to as graphite fibers; however, only very high modulus carbon fibers with three-dimensional graphite structure can properly be called graphite fibers. Because carbon fibers have extremely high specific strength and modulus when compared to other engineering materials, they are predominantly used in weight critical applications. The specific strength and stiffness of commercially available carbon fibers can be double other reinforcing fibers such as Kevlar and S-glass, and they exceed metals by an order of magnitude (Fig. 1). When designing with carbon fiber composites, strength and modulus can be oriented optimally to minimize final part weight. In addition to strength and stiffness, carbon fibers possess excellent fatigue strength, vibration damping characteristics, thermal resistance, and dimensional stability. Carbon fibers also have good electrical and thermal conductivity and chemical inertness, except to oxidation.

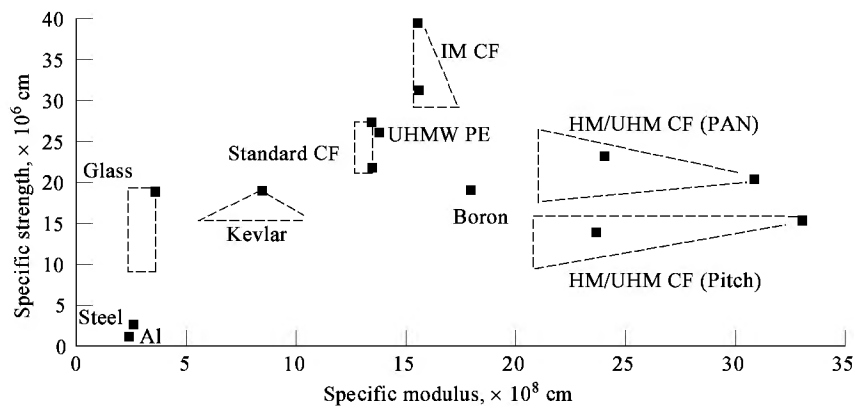


Fig. 1. Specific strength and Young's modulus of various engineering materials where CF = carbon fiber; HM/UHM = high modulus/ultrahigh modulus ; IM = intermediate modulus; and UHMW PE = ultrahigh molecular weight polyethylene.

The element carbon has two low density allotropes, diamond and graphite, with strong covalent bonding between carbon atoms. The microstructure of carbon fibers is based on the hexagonal layer structure of graphite; however, commercial carbon fibers lack true three-dimensional order between layer planes. This incompletely ordered graphite structure is termed graphene, or turbostratic, graphite (see CARBON, NATURAL GRAPHITE). The strong sp^2 bonding within graphite layer planes results in the highest absolute modulus and theoretical tensile strength of all known materials (1). Transverse properties are significantly lower than axial properties as graphite layers are held together by weak dispersive bonds resulting in low shear modulus and cross plane Young's modulus and strength. The physical and mechanical properties of carbon fibers are primarily determined by the axial orientation of the carbon fiber layer planes (Figs. 2 and 3) and the degree of crystalline perfection. Both can be studied through x-ray diffraction. The detailed structural characteristics of carbon fibers have been investigated (3–8).

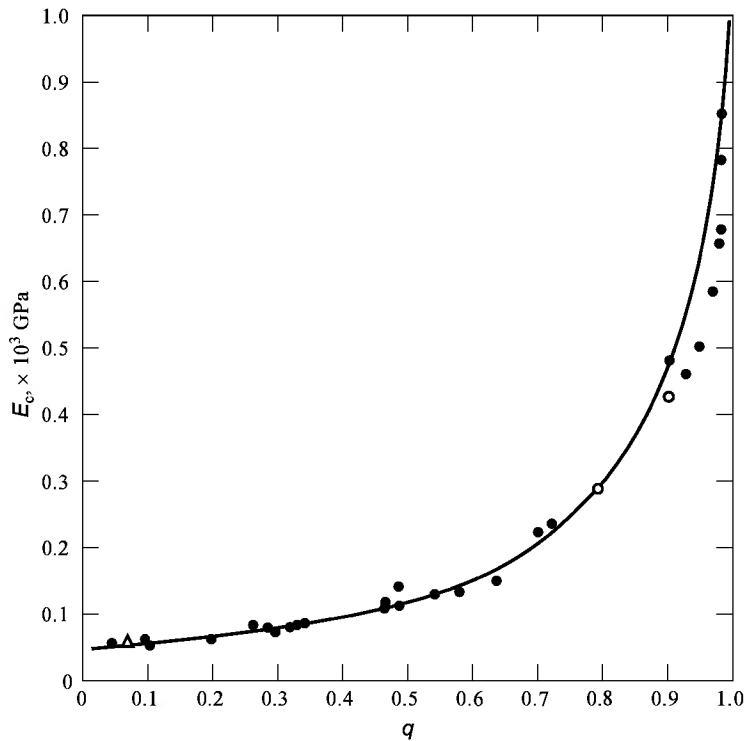


Fig. 2. Young's modulus corrected for porosity E_c as a function of preferred orientation q , curve is based on theoretical model where ● = rayon-based fibers; ○ = PAN-based fibers; and △ = pitch-based fibers (2). To convert GPa to psi, multiply by 145,000.

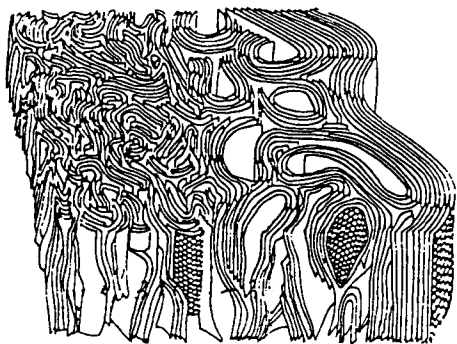


Fig. 3. Schematic illustration of PAN-based carbon fiber microstructure based on microscopic observations (3).

Thomas Edison (9) first intentionally produced carbon filaments by pyrolyzing cotton for incandescent lamp filaments in 1878. More than 80 years later the tremendous strength potential of carbon fibers was demonstrated by growing graphite whiskers with strengths of 20 GPa (2.9×10^6 psi) and extensional moduli of 800 GPa (1.2×10^8 psi) (10). The first commercial continuous carbon fibers were produced in the 1950s by carbonizing synthetic rayon for high temperature missile applications. However, the conversion of rayon to carbon fiber was inefficient because of low carbon yields and resulted in carbon fibers with poor mechanical properties. In the early 1960s in Japan (2) and in England (11), a more efficient process for producing high strength carbon fibers using PAN precursor was demonstrated. This general process is used today for more than 90% of commercial carbon fiber production. During the past 20 years this process has been optimized to improve efficiency and to increase fiber strength, modulus, strain to failure, and handleability.

During the 1970s efforts focused on reducing fiber cost through the use of a less expensive pitch precursor. Union Carbide commercialized low modulus pitch carbon fibers based on isotropic pitch precursor and a family of high modulus carbon fibers based on liquid crystal pitch precursors. Unfortunately deficiencies in fiber compression strength and high cost of purifying the liquid crystalline pitch precursor have limited the acceptance and growth of high modulus pitch carbon fibers. Current research to develop low cost carbon fiber includes growing carbon filaments via vapor deposition of carbon from gases such as carbon monoxide, methane, or benzene on metal catalysts (12).

Carbon fibers are generally typed by precursor such as PAN, pitch, or rayon and classified by tensile modulus and strength. Tensile modulus classes range from low (<240 GPa), to standard (240 GPa), intermediate (280–300 GPa), high (350–500 GPa), and ultrahigh (500–1000 GPa). Typical mechanical and physical properties of commercially available carbon fibers are presented in Table 1.

Table 1. Mechanical and Physical Properties of Carbon Fibers^a

Property	PAN, standard-gra de	PAN-IM	PAN-HM	PAN-UH M	Pitch HM	Pitch UHM
tensile strength, GPa ^b	3.5–4.8	4.1–7.0	1.7–4.7	1.7–3.9	2.4–3.0	2.2–3.3
tensile modulus, GPa ^b	230–240	280–300	350–480	500–600	380–520	550–827
elongation at break, %	1.5–2.1	1.5–2.4	0.4–1.4	0.3–0.7	0.4–0.6	0.27–0.5
density, g/cm ³	1.77–1.81	1.79–1.82	1.70–1.90	1.93–2.00	2.00–2.14	2.15–2.20
filament diameter, μm	7	5	4.5–6.5	4.5–6.5	10	10
carbon, wt %	92–96	93–96	99+	99+	99+	99+
axial resistivity, μohm·m	14–18	14	6.5–10	6.5	7–8.5	2–5
axial thermal conductivity, W/(m·K)	8–14	15	70–105		120–185	360–640
axial coefficient of thermal expansion at 21°C, ppm/°C	–0.6	–0.75	–1.15		–1.3–1.4	–1.45
standard filament counts	3K/6K/12K	6K/12K	3K/6K/12K	3K/6K	0.5K/1K/2K/4K	0.5K/1K/2K

^a Data from the following technical data sheets: PAN fibers: Amoco Performance Products, Asahi Kasei, BASF Structural Materials, Courtaulds-Grafil, Hercules, Mitsubishi Rayon, Toho Beslon, Toray; Pitch fibers: Amoco Performance Products, Mitsubishi Kasei, Tonen Corp.

^b To convert GPa to psi, multiply by 145,000.

Producers of PAN-based carbon fiber include Toray, Toho Beslon, Mitsubishi Rayon, and Asahi Kasai Carbon in Japan; Hercules, Amoco Performance Products, BASF Structural Materials, Fortafil (Akzo), and Mitsubishi Rayon in the United States; and Akzo, Sigrí, and Soficar in Europe. Primary suppliers of high performance pitch-based carbon fibers include Amoco Performance Products, Mitsubishi Kasai, and Tonen Corp.

Carbon Fiber Manufacturing Processes

More than 95% of current carbon fiber production for advanced composite applications is based on the thermal conversion of polyacrylonitrile (PAN) or pitch precursors to carbon or graphite fibers. Generally, the conversion of PAN or pitch precursor to carbon fiber involves similar process steps; fiber formation, ie, spinning, stabilization to thermoset the fiber, carbonization–graphitization, surface treatment, and sizing. Schematic process flow diagrams are shown in Figure 4. However, specific process details differ.

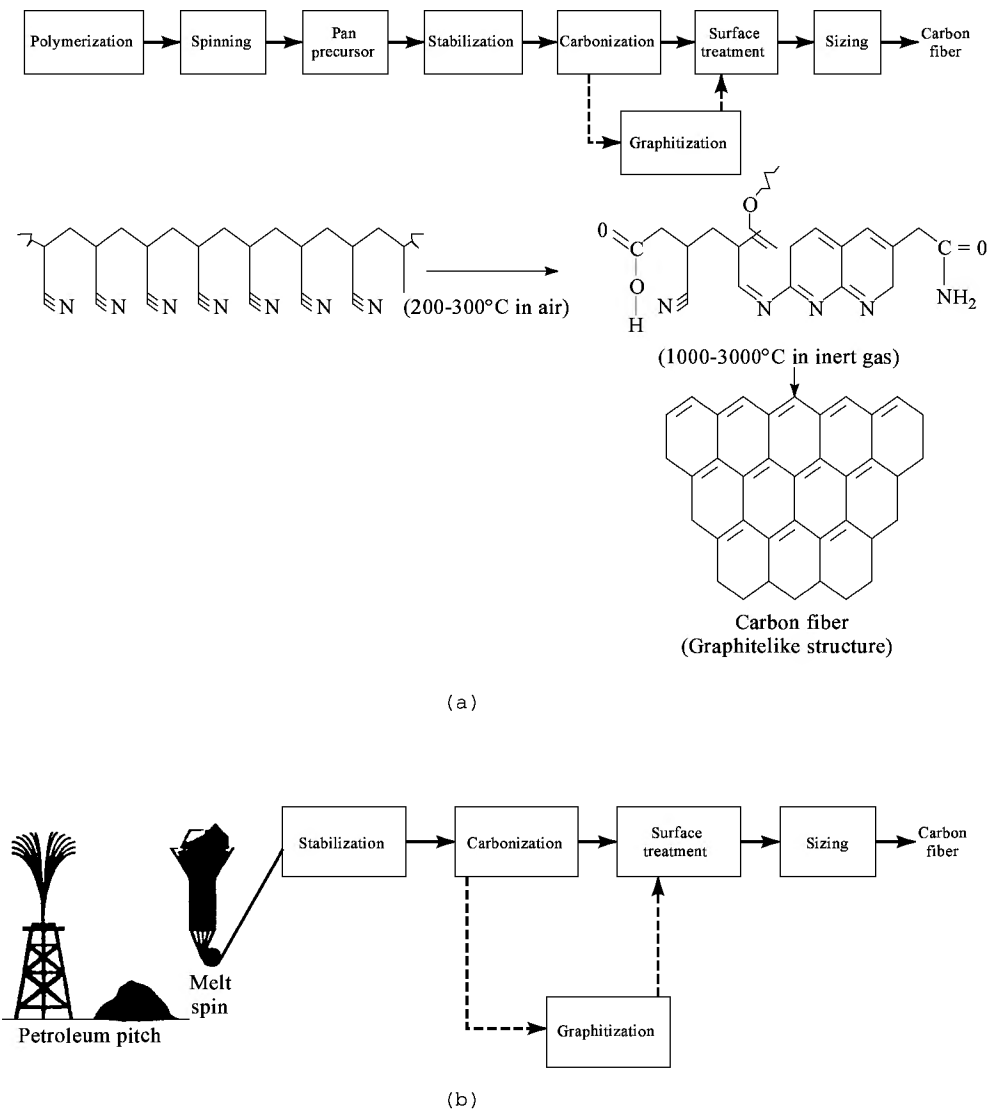


Fig. 4. Process flow diagrams for (a) PAN-based and (b) pitch-based carbon fiber processes.

POLYACRYLONITRILE CARBON FIBER PROCESS

After it was demonstrated that PAN fibers were suitable for conversion to high modulus carbon fibers (2), work was advanced in the late 1960s in England (11) and the early 1970s in the United States to devise large-scale continuous carbon fiber manufacturing processes based on PAN precursor. PAN became the predominant carbon fiber precursor for several reasons. First, it was readily available. Commercial textile acrylic processes were well-established in England and Japan and could be modified to produce specialty carbon fiber-grade acrylic fibers. The modified acrylic process provided consistent precursor of relatively high purity. Secondly, when carbonized, PAN provides a high carbon yield compared to rayon, typically 55% vs ~20% for rayon resulting in improved process conversions. Also, the mechanical properties of PAN-based carbon fibers were significantly improved over previous rayon-based carbon fibers. PAN precursor composition, structure, and quality predetermine carbon fiber manufacturing conditions, and to a large extent the quality and mechanical properties of the resultant carbon fiber.

The exact composition of PAN polymer used for carbon fiber precursor varies from company to company and is commonly considered to be a trade secret. Patent literature (13) suggests that copolymers with greater than 90% acrylonitrile (AN) with small amounts of comonomers such as methyl acrylate [96-33-3], methyl methacrylate [80-62-6], methylvinylpyridine, methacrylic acid, or itaconic acid are predominantly used. The comonomer serves two purposes. First, the comonomer increases thermal reactivity and broadens the sharp exothermic reaction that occurs during stabilization of PAN, increasing stabilization rates, and providing better thermal control of the process. Secondly, it tends to reduce the strong intermolecular bonding that occurs in PAN homopolymer because of the polar nitrile group, and increases fiber stretchability (see ACRYLONITRILE POLYMERS).

Conventional suspension or solution polymerization technology is used to produce a polymer that is then converted into precursor fiber using wet, dry-jet, dry, or more recently melt-assisted spinning. In the first three spinning processes a dilute solution of polymer in DMSO, DMF, DMA, nitric acid, or aqueous salt solutions such as sodium thiocyanate, zinc chloride, or sodium chloride is spun into a coagulation bath, typically a similar solution at lower concentration and/or lower temperature, or quench chamber where the fiber is precipitated from solution. Melt-assisted spinning of PAN is accomplished by pressurized heating of a concentrated PAN–water–solvent mixture to form a single-phase melt that is extruded into a spinning chamber where the water and solvents are vaporized under controlled conditions (14,15). Both spinning and coagulation conditions must be finely controlled because it is during these processes that the shape and internal structure of the precursor is formed (16).

The precursor fiber is subsequently washed and stretched to the low tex (denier) required for carbon fiber processing. Stretching also imparts considerable orientation to the polymer molecules and provides the basis for the highly oriented carbon structure that forms after carbonization. Special care is taken to avoid contamination or impurities that may form strength reducing flaws in the carbon fiber.

Stabilization. Prior to carbonization the precursor fiber must be chemically thermoset to lock in molecular orientation and increase carbon yields. For PAN precursors this generally involves converting the linear PAN polymer to a more thermally stable cyclized ladder polymer by oxidizing at temperatures of 200–300°C for periods of 30 minutes to two hours. The molecular orientation developed during spinning and drawing is locked in place by stretching, or at least restraining the fiber from shrinking during stabilization. Stabilization reactions are complex (17–20) but typically involve cyclization of the pendent nitrile groups, dehydrogenation, oxidation, and intermolecular cross-linking through oxygen and nitrile linkages (Fig. 5). Cyclization can be initiated either by free-radical (homopolymer), or ionic mechanisms as is the case with most carbon fiber precursors. These reactions are exothermic and must be done under controlled conditions to avoid thermal runaway and undesirable side reactions.

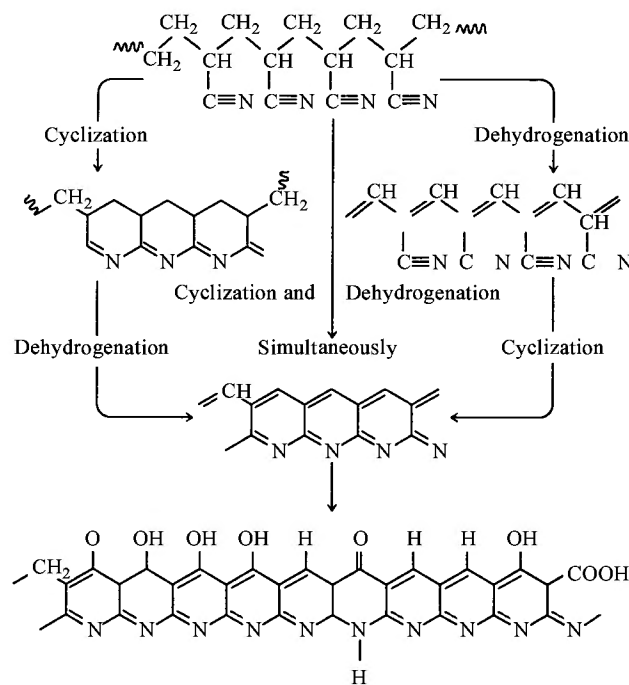


Fig. 5. Chemical reactions occurring during stabilization of PAN precursor (13).

During stabilization fiber density increases as a more condensed ladder polymer structure is formed. The degree of stabilization can be described by fiber density or oxygen content. Fully stabilized fibers have densities exceeding about 1.35 g/cm³ and oxygen contents exceeding 6% by weight (21,22). At low stabilization temperatures oxidation is primarily reaction limited. At higher temperatures, the process becomes limited by the diffusion of oxygen to the core of the fiber, and an oxygen gradient develops from the fiber surface to the core. This inhomogeneous structure is clearly visible in microtomed cross sections of stabilized fiber and is commonly referred to as skin-core structure.

Commercially, stabilization is accomplished by controlled heating in air at temperatures of 200–300°C. A variety of equipment has been proposed for continuous stabilization. One basic approach is to pass a fiber tow through heated chambers for sufficient time to oxidize the fiber. Both Mitsubishi and Toho patents (23,24) describe similar continuous processes wherein the fiber can pass through multiple ovens to increase temperature and reaction rate as the thermal stability of the fiber is increased. Alternatively, patents have described processes where the fiber passes over hot rolls (25) and through fluidized beds (26) to provide more effective heat transfer and control of fiber bundle temperature.

A number of patents describe accelerators that will reduce the time required for stabilization (24,27,28). The accelerators are often inherent to the polymer or precursor but may be added to the gas phase during stabilization. For example, it is common to have an acid group present as comonomer such as itaconic acid [97-65-4] or methacrylic acid [79-41-4]. The acid groups provide initiation sites for cyclization. Alternatively, the stabilization atmosphere composition can be modified to accelerate stabilization (29).

Carbonization. Stabilized precursor is converted to carbon fiber by controlled heating to temperatures exceeding 1000°C in a nonoxidizing environment under tension. Standard-grade, 240 GPa (35 × 10⁶ psi), PAN carbon fibers are generally heated to 1200–1400°C. Higher modulus fibers can be produced by increasing carbonization temperatures. Some very high modulus fibers, such as BASF GY70 fiber, are produced at temperatures approaching 3000°C. Fiber composition and structure change significantly during carbonization as the fiber is converted from a relatively low strength textile polymer with elongation of approximately 10% to a relatively brittle ceramic fiber with elongation ranging from 1–2%. Carbon content increases as hydrogen, oxygen, and nitrogen are evolved as shown in Table 2.

Table 2. Effect of Peak Carbonization Temperature on PAN Carbon Fiber Composition, wt %

Temperature, °C	Carbon	Nitrogen	Oxygen	Hydrogen
700	71	21	6	2
900	77	17	5	1
1100	86	12	2	
1300	95	5		
2000+	99+			

Decomposition gases are generated in various forms as water, ammonia, hydrogen cyanide, carbon monoxide, carbon dioxide, hydrogen, nitrogen, and various higher molecular weight nitrile gases and tars. Approximately 40–50% of the fiber mass is lost during carbonization. The chemical changes that occur during carbonization have been described (20,30).

Structurally, the carbon layer planes become more compact and aligned as indicated by increasing fiber density and modulus. Structural changes progress through three phases (31): (1) initial formation of a graphene layer plane structure. This generally occurs at temperatures ranging from 400 to 1000°C (Zone A in Fig. 6). Strength, modulus, and conductivity increase rapidly as the oxidized polymeric fiber is converted to a predominantly carbon fiber; (2) from 1000°C to 1500°C (Zone B) graphitic crystal growth and alignment begin to take place. Aside from the loss of nitrogen, few chemical changes occur. Modulus development is relatively difficult in this temperature range; (3) at temperatures exceeding 1500°C, atomic mobility is increased and crystal growth and molecular alignment occur easier as indicated by the increase in the slope of the modulus versus temperature curve. As carbonization temperatures increase beyond 1500°C the growth in crystallite size results in a more flaw-sensitive structure and fiber tensile and compressive strength may decrease because of defects such as trace metal contaminants, surface flaws, or shear failure across misaligned crystallites.

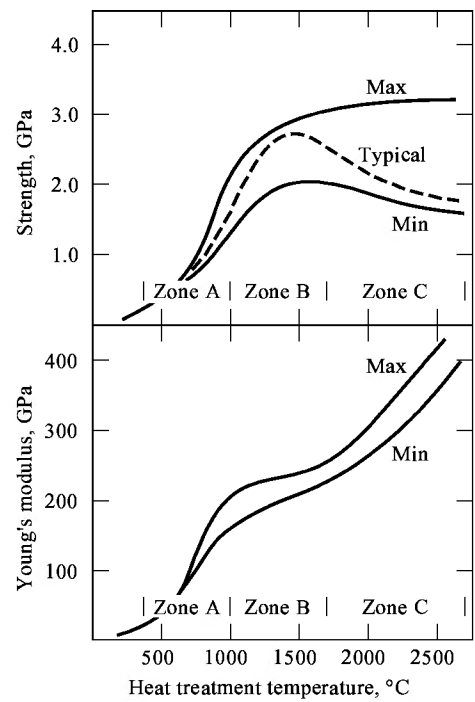


Fig. 6. Each of carbonization temperature on PAN-based carbon fiber strength and modulus (31). To convert GPa to psi, multiply by 145,000.

In the initial stage of carbonization, it is critical to control the off-gases that evolve from the fiber as it is heated. Excessive heating rates result in void formation, structural disruption, and lower carbon fiber properties.

Commercial carbonization is done by passing the stabilized precursor through high temperature furnaces blanketed with a nonoxidizing gas. The furnace end seals are typically pressurized to prevent the ingress of oxygen. Often two furnaces are used (32,33); a precarbonization furnace to control the decomposition gases generated below 1000°C better, and a higher temperature carbonization furnace to control final carbon fiber properties. The temperature profiles and residence times are optimized to control carbon fiber properties. Compared to the stabilization process that takes from 30 minutes to two hours, the carbonization process is relatively fast with residence times at peak temperatures on the order of minutes.

Further heat treatment in excess of 2000°C is referred to as graphitization. Fiber structure further densifies as molecular packing and orientation increase. At temperatures of 3000°C or above, the fiber structure begins to approach a truly graphitic structure with three-dimensional order. Typically, fiber strain to failure decreases as the carbonization temperature exceeds 1500°C because of reaction of impurities with the carbon fiber and the development of an increasingly flaw-sensitive graphitic structure (31,34)

Surface Treatment. At the completion of carbonization, the carbon fiber has a low energy graphene surface that does not bond very well to polymeric matrices, such as epoxies, bismaleimides, and thermoplastics, or metals. Surface treatments alter the fiber surface chemistry, increase surface energy improving fiber wettability, and increase surface roughness to provide sites for mechanical interlocking. Most treatment processes are oxidative and can increase fiber surface oxygen content from ~5 atom % oxygen:carbon ratio present after carbonization to 12–25% (35). Oxidation will also etch and roughen the fiber surface for improved mechanical interlocking with matrices. Consequently, excessive surface treatment depresses fiber tensile strength because of surface defects and can in fact reduce composite interfacial properties by creating a brittle, flaw-sensitive interface. High modulus fibers, carbonized at temperatures exceeding 1800°C possess a more graphitic (inert) fiber surface and must be treated at higher energy to improve interfacial bonding. Following surface treatment the interlaminar shear strength of standard-grade carbon fiber–epoxy composite typically increases from 50–70 to 90–140 MPa and high modulus carbon fiber–epoxy composites from 30–50 to 70–90 MPa (1 MPa = 145 psi). The improvement in composite properties that results from surface treatment is well documented (36–38).

Oxidative surface treatment processes can be gaseous, ie, air, carbon dioxide, and ozone; liquid, ie, sodium hypochlorite, and nitric acid; or electrolytic with the fiber serving as the anode within an electrolytic bath containing sodium carbonate, nitric acid, ammonium nitrate, ammonium sulfate, or other electrolyte. Examples of electrolytic processes are described in the patent literature (39,40)

Toray has also described a combination of electrolytic oxidation with gaseous deactivation in a reducing atmosphere at temperatures ranging from 600 to 900°C for high strength carbon fibers (41,42). Plasma treatments have also been patented and offer the additional advantage of tailoring the fiber surface chemistry by adjusting plasma composition (43).

It is critical that surface treatment conditions be optimized to composite properties since overtreatment as well as undertreatment will degrade composite properties. Typically composite interlaminar shear strength (ILSS), in-plane shear, and transverse tension are used to assess the effectiveness of surface treatment. More recently damage tolerance properties such as edge delamination strength, open hole compression, and compression after impact have become more important in evaluating the toughness of composite parts.

Sizing. After surface treatment the fiber tow is coated or sized to protect it from damage during post-processing steps such as winding, weaving, and pre-pregging. The size is generally matched for compatibility with end use matrix. Typical sizes are epoxy, polyester, nylon, urethane, or polycarbonate that can be applied from solution or emulsion. Size content for continuous filaments varies from 0.7 to 1.2% by weight and can be as high as 7% for chopped fiber products. Sizes can also improve wetting of the fiber surface by the matrix resin but generally do not chemically bond the fiber to the matrix.

Following sizing, the continuous carbon fiber tows are wound onto precision packages of various sizes from 1 to 6 kg depending on customer preference. The final bobbins are relatively stable and can be stored at room temperature for periods of one year or more. With longer storage times epoxy sizes are prone to advancement resulting in a much stiffer tow with reduced spreadability.

PITCH-BASED CARBON FIBER PROCESS

The use of pitch as a potentially inexpensive alternative to PAN precursor began in 1965 when it was demonstrated (44) that carbon fibers could be produced from the pyrolysis residue of poly(vinyl chloride). Since the pitch-based carbon fiber (PBCF) process uses inexpensive raw materials that have approximately 50% higher carbon yield than PAN (85% vs ~55%), it is more efficient and has the potential to reduce carbon fiber cost significantly. Conversion of a pitch precursor fiber to carbon fiber is similar to the PAN-based carbon fiber process. The pitch precursor is thermoset by oxidation in ozone or air, then carbonized at temperatures ranging from 500 to 1500°C, and graphitized at temperatures above 2000°C. The carbonized–graphitized fibers are surface treated, sized, and wound on precision packages. Initially, carbon fibers using isotropic pitches that develop little preferred molecular orientation during spinning were produced (44). The resultant fibers possessed low modulus 56 GPa (8.1 × 10⁶ psi) and strength of 1.8 GPa (261,000 psi). Isotropic pitch carbon fibers of this type were first commercially produced by Kureha Chemical Co. in Japan and more recently by Ashland.

To improve mechanical properties, increased axial molecular orientation was required. Union Carbide workers under government contract worked on

a process to convert commercial pitches thermally to liquid crystal, or mesophase, which readily orients during spinning (45). The highly oriented mesophase precursor was graphitizable and resulted in carbon fibers with higher modulus than PAN fibers treated to the same carbonization temperature. Along with high modulus potential, the initial mesophase carbon fibers demonstrated relatively high strength and excellent thermal and electrical conductivity. Union Carbide patented a pitch-based carbon fiber and several key process elements (46–48), then subsequently transferred this technology to Amoco. Several Japanese companies have continued the development of pitch-based carbon fibers, such as Tonen, Mitsubishi Kasai, and Kashima Oil.

One key step in the PBCF process is the conversion of an isotropic petroleum or coal-tar pitch to a mesophase pitch by separating or converting the low molecular weight components from the planar aromatic molecules that tend to orient under proper conditions. A simplified phase diagram for the complex pitch composition (Fig. 7) (49) shows that conversion can be done by thermally treating the pitch at elevated temperatures (typically from 350–500°C) under inert atmosphere. Alternatively solvents can be used to dissolve the low molecular weight disordering components leaving an insoluble fraction of more aromatic species that will form mesophase (50). In other processes (51), a coal-tar or petroleum pitch is hydrogenated, then heat treated to thermally strip the low molecular weight species. The partial hydrogenation of the aromatic molecules helps avoid the formation of particulate graphitic defects during carbonization that limit strength development.

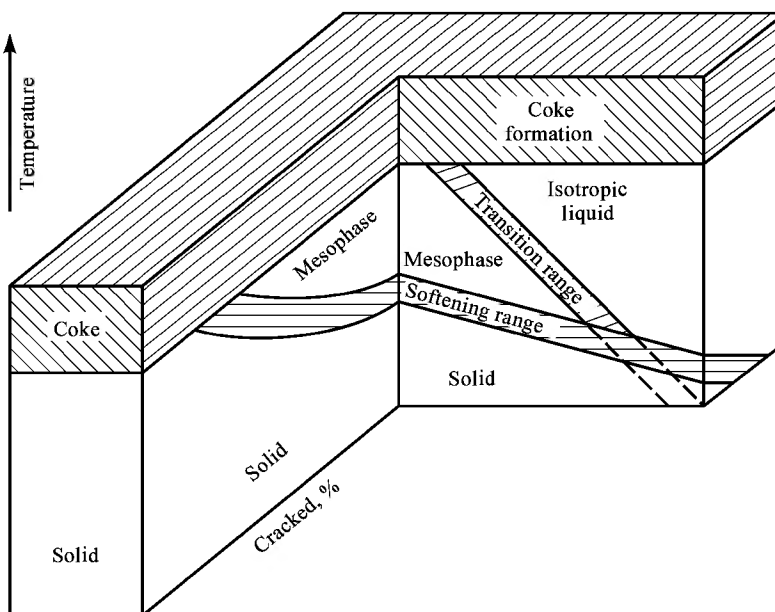


Fig. 7. Three-dimensional pseudophase diagram of an oil or coal-tar pitch (49).

The mesophase pitch is then extruded and melt spun through spinnerettes into fibers. The flow pattern of the mesophase during fiber formation has a strong influence on the morphology of the fiber (52–54) and can result in fibers with radial, onion-skin, or random microstructures. Commercially available PBCFs have a round cross section, but this can be easily modified by changing the cross section of the spinnerette holes. Multilobal and C-shaped fibers have been produced with exceptional mechanical properties (55).

After spinning, the fibers are thermoset by oxidation at temperatures below the softening point of the pitch, typically 200–300°C, and carbonized and graphitized in a nonoxidizing atmosphere at temperatures between 2500 and 3000°C. The high degree of molecular orientation induced during spinning is maintained during stabilization and increased through graphitization. Higher graphitization temperatures result in increased fiber modulus and tensile strength because of increased crystallite growth and preferred orientation.

Pitch-based carbon fibers tend to be more graphitizable than PAN-based carbon fibers and can be processed to higher modulus. When pitch and PAN fibers with equivalent moduli are compared, the pitch-based fiber has a more graphitic structure, higher density, and greater electrical and thermal conductivity (Table 1). Unfortunately, the higher level of graphitic perfection results in weak transverse fiber properties and relatively poor fiber compression performance. These characteristics limit use in advanced structural applications. Research aimed at adjusting the microstructure of pitch-based fiber has shown that compression strength can be increased but the level of PAN-based fibers has not yet been reached.

Currently the cost of PCBFs is comparable to PAN-based fibers because of limited manufacturing capacities and the high cost of preparing a suitable mesophase precursor. Pitch-based fibers do not currently compete in the broad aerospace and recreation markets primarily as a result of poor compression strength (56). Ultimately the PBCF market will grow in areas that take advantage of the excellent thermal and electrical properties, such as thermal management in electronics and industrial heat-transfer applications.

Carbon Fiber Property Development

The Young's modulus of carbon fibers is primarily determined by the relative orientation of the hexagonal layer planes to the carbon fiber axis. Increasing precursor molecular orientation, tension applied during processing, or carbonization–graphitization temperatures directly increase carbon fiber modulus. Commercially available carbon fibers span a broad range of modulus from 240 GPa (35×10^6 psi) to approaching the theoretical limit of graphite, approximately 1020 GPa (1.5×10^8 psi). A typical example of the relationship between carbonization temperature and resultant carbon fiber modulus is shown in Figure 6. The specific test procedure must be considered when comparing reported fiber modulus because carbon fiber strains harden, increasing in modulus by up to 10% under loading.

Theoretically, carbon fiber strength potential is also determined by molecular orientation. Bond strength calculations estimate the ultimate strength potential of graphite to be approximately 150 GPa (22×10^6 psi) (1). Practically however, strength is limited by flaws or defects such as pores, contaminants, coalescence, ie, fiber fusion, or structural imperfections that reduce strength to a fraction of this theoretical value (57). The impact of flaws on fiber strength is clearly demonstrated by gauge length tests that show fiber strength increases significantly at shorter test lengths (58). During the past 10 years optimization of the precursor and carbon fiber process to reduce flaws has increased fiber strength from approximately 3 to 5–7 GPa (7 GPa $\approx$ 1,000,000 psi). Many high strain carbon fibers possess strain to failure exceeding 2%. Investigation of the relationship between strength and modulus generally show that as carbonization temperatures exceed 1400–1500°C fiber strength is reduced because of reaction of trace contaminants and the increased flaw sensitivity of the higher modulus fiber (34).

Density. The density of carbon fibers ranges from approximately 1.5 g/cm³. For PAN-based carbon fibers the values are approximately 1.77 g/cm³ for standard modulus (240 GPa modulus) and approach 2.0 g/cm³ for ultrahigh modulus grades exceeding 500 GPa (72.5×10^6 psi). Densities of pitch-based carbon fibers are higher than PAN, ie, between 2.05–2.20 g/cm³. Carbon fiber density is typically less than that of single-crystal graphite, 2.26 g/cm³, because of the imperfect packing of the graphene layer planes and because of internal microporosity present within polymer-derived carbon fibers. These pores are very small, generally less than 3 nm in diameter, and are not penetrated by the helium or mercury used in commercial pycnometers or visible under scanning electron microscopes. Specific information on the size and distribution of porosity can be obtained using small-angle x-ray diffraction that would suggest a microporosity of PAN fibers ranging from ~2–5%. By comparing the interlayer spacing to the geometric density it is

possible to calculate a relative pore volume that includes both macro- and microporosity. This type of comparison shows that standard PAN carbon fibers with a density of 1.77 g/cm³ and interlayer spacing of 0.35 nm have a pore volume of approximately 20%. The densities of various types of commercially available carbon fibers are compared in Table 1.

Electrical and Thermal Conductivity. During the transformation from polymeric fiber to carbon or graphite fiber the electrical conductivity is dramatically increased from a typical polymeric insulator to a very good conductor, spanning more than 10 orders of magnitude. This change occurs as the polymeric fiber increases in carbon content and crystalline perfection. Concurrently, thermal conductivity is increased in direct relation to electrical conductivity as shown in Figure 8, which also illustrates the impact of fiber modulus and carbonization temperature on electrical conductivity and thermal conductivity. Generally, higher carbonization temperatures increase the concentration of mobile electrons and reduce the energy gap for conductivity. More complete descriptions of the effect of thermal treatment on electrical conductivity of PAN and pitch fibers have been given (60–62). Carbon fibers exhibiting low and high conductivity are utilized in specialized applications. For example, carbon fibers with relatively low conductivities, ie, semiconductive (63), can be used for static dissipation applications, and standard-grade carbon fibers with good conductivity can be used in plastics for electromagnetic shielding.

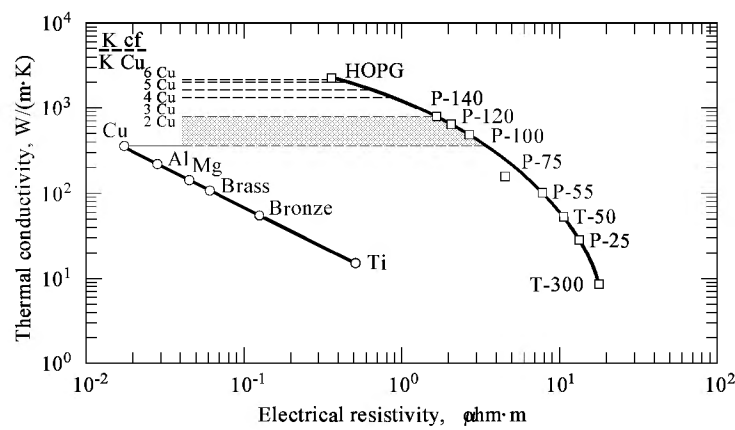


Fig. 8. Comparison of electrical and thermal conductivity of PAN- and pitch-based carbon fiber to metals, where P = pitch, T = Thornel, and HOPG = highly oriented pyrolytic graphite (59).

Mechanical Properties and Stability at Elevated Temperature. One increasingly important characteristic of carbon fibers is their excellent performance at elevated temperatures. Strength tested in an inert environment remains constant or slightly increases to temperatures exceeding 2500°C. Amoco's high modulus pitch carbon fiber P-50 maintains approximately 80% of room temperature modulus at temperatures up to 1500°C, then decreases more rapidly to 30% at 2800°C (64). The rapid decrease in modulus is a result of increased atomic mobility, increasing fiber plasticity.

Although carbon fibers retain their excellent mechanical properties at elevated temperatures in an inert environment or in a vacuum, they are reactive with oxygen at temperatures exceeding 300°C forming carbon monoxide and carbon dioxide. Oxidative stability is related to the degree of graphitization and impurity level, especially alkali metals that catalyze graphite oxidation reactions. High modulus fibers have improved thermal oxidative stability (TOS) over low modulus fibers because of a lower concentration of reactive edge sites on the fiber surface. Oxidation mechanisms present in graphitized carbons, most of which are also applicable to carbon fibers, have been described (65,66).

There are two mechanisms of PAN-based carbon fiber oxidation dependent on oxidation temperature ((67,68). At temperatures below 400°C, oxygen diffuses into the fiber and attacks at pores resulting in significantly increased fiber surface area. At higher temperatures impurities catalyze the oxidation reaction.

Most recent studies (69) on elevated temperature performance of carbon fiber-based composites show that the oxidation resistance and elevated temperature mechanical properties of carbon fiber reinforced composites are complex and not always directly related to the oxidation resistance of the fiber. To some extent, the matrix acts as a protective barrier limiting the diffusion of oxygen to the encased fibers. It is therefore critical to maintain interfacial bonding between the fiber and the matrix, and limit any microcracking that may serve as a diffusion path for oxygen intrusion. Since interfacial performance typically deteriorates with higher modulus carbon fibers it is important to balance fiber oxidative stability with interfacial performance.

Quality Control and Specifications

Typically the quality control philosophy used for carbon fibers is based on consistent precursor and tight control of processing parameters such as linespeed, temperature, and gas flow at each process step. Process control documents (PCDs) are used by some aerospace customers to assure consistent process conditions. Fiber physical and mechanical properties are tested statistically, along with some composites testing to assure the product meets specifications. Common fiber tests include yield (denier), density, strand strength, strand modulus, and size level. Composite tests include strength, modulus, and interlaminar shear strength (ILSS). Until recently each carbon fiber producer established internal test procedures to assure product quality consistent with end user requirements. In 1990 the Suppliers of Advanced Composite Materials Association (SACMA) established industry wide standards for carbon fiber test methods (70).

Most users require extensive composite qualification testing programs to assure acceptable end use product properties. The magnitude of the qualification depends entirely on the end use requirements and may range from extensive testing of laminates and final parts made from several production lots of fiber, to a single lot laminate evaluation or test coupon verification of properties.

Health and Safety Factors

Safety concerns in handling carbon fibers fall into three categories: dust inhalation, skin irritation, and electrical shorting of equipment. Additionally, the protective finish, or size, which is applied to the fiber may necessitate additional safety precautions. The most common sizes are epoxies that may contain cross-linking or curing agents that produce severe skin reactions. Groups such as SACMA provide general information on the safety of carbon fibers and composites. However, since carbon fiber sizes are specially formulated to match end use requirements, it is best to consult with the Material Safety Data Sheet (MSDS) available from the suppliers for specific handling requirements.

Dust Inhalation. During processing, fine carbon filaments (5–10 μm in diameter) may break and be circulated in the air as a carbon dust that can be inhaled by operators. Studies (71) show the fibers are too large to represent a respiratory health risk; however they often create discomfort, and a protective mask is recommended when working in areas where carbon fiber dust is present.

Skin Irritation. Fine broken filaments often irritate the skin, occasionally causing transient itching and rashes. The back of hands and wrists and neck areas tend to be most sensitive. Protective clothing and barrier skin creams help prevent the fiber from reaching the skin and causing discomfort.

Electrical Hazards. Because carbon fibers are conductive, the airborne filaments can create serious problems shorting out electrical equipment. The best option is to locate sensitive equipment in clean rooms outside of areas where carbon fiber is being processed. If this is not possible, electrical cabinets must be effectively sealed to prevent contact with carbon fibers. A filtered air-positive purge provides additional protection for sensitive equipment.

Applications of Carbon Fibers

With excellent specific stiffness and strength, carbon fibers are ideally suited to applications where weight reduction results in significant performance and cost advantages. Initially military aerospace, space, and recreation were primary markets. The relatively high cost of the fiber prevented penetration into more cost-sensitive applications. Current 1992 prices of standard and intermediate modulus PAN-based carbon fibers such as BASF G30-500 and G40-800, range from \$20–60 kg depending on filament count and order volume. Higher modulus products are even more expensive with ultrahigh modulus pitch-based fibers such as Amoco's P-100 exceeding \$2000 kg. More recently carbon fiber composite applications have diversified into automotive, ie, brake linings, drive shafts, springs, wheels, and structural components for racing cars; aircraft engines; recreation, ie, fishing rods and reels, tennis and racquetball racquets, golf club shafts, baseball bats, hockey sticks, oars, paddles, sailing masts, skis, etc; electrical shielding and radar; absorption; medical, ie, x-ray tables and prosthetic devices; and music applications, ie, speaker cones and musical instrument components.

The use of carbon fibers in new applications will continue to grow as fiber costs are reduced further. Toray estimates that the global market will increase by about 64° 0 by 1995 to almost 9500 t. More conservative estimates based on the recent cutbacks in military programs suggest annual growth of 5–8° 0 from 1991 through 1994, then increasing to average a 10° 0 annual growth over the next 10 years (72). A large part of this growth is based on increased usage of carbon fibers in new commercial aircraft such as the Boeing 777. Estimated prepreg usage per 777 is 4000 kg per aircraft (73).

Further reduction in the price of carbon fibers may enable penetration into the automotive market. A primary carbon fiber producer has announced that prices will drop to 700 yen kg (~\$6.80 lb) by 1995 (73) and that cooperative development efforts with a main Japanese automobile producer are underway. Development for use in construction, such as cement and cable reinforcement, and marine applications will result in sustained growth volume through the early twenty-first century.

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CARBONATED BEVERAGES

The carbonated beverage has its origin in the study of mineral waters in Europe in the sixteenth century. In the late eighteenth century, artificial mineral waters were investigated for their medicinal properties both in Europe and America. The first commercial artificial mineral water was manufactured in Europe during the 1780s and in America in the early 1800s.

Flavored carbonated beverages, or soft drinks, were developed by apothecaries and chemists in the early nineteenth century by the addition of flavored syrups to fountain-dispensed carbonated water. The introduction of proprietary flavors began in the late 1880s. Charles H. Hires introduced his root beer extract in 1876, Vernors's Ginger Ale was marketed by James Vernor in 1880, R. S. Lazenby perfected the formula for Dr. Pepper in 1885, and John S. Pemberton developed the formula for Coca-Cola in 1886. Brad's Drink was introduced in 1896 and was later renamed Pepsi-Cola in 1898.

Early bottling of flavored carbonated beverages was limited by spoilage, poor flavor, and color stability. Improvements and innovations in bottling equipment, glass manufacturing, stable flavors and ingredients, crown closures, and transportation resulted in the rapid expansion of the bottled soft drink industry. Soft drinks consist of carbonated water, nutritive or nonnutritive sweeteners, acidulants, preservatives, flavors, juices, and color.

Consumption

The consumption of carbonated beverage has risen steadily since they were first introduced. Annual per capita consumption of soft drinks in the United States was approximately 16 ounces (<0.5 L) in 1860 and is estimated to be 47.5 gallons (~180 L) in 1990 (Fig. 1). Although the consumption of soft drinks has increased, the number of soft drink plants has dropped steadily from 2258 in 1975 to 780 in 1991. Production of soft drinks has increased from 2.6 billion cases in 1975 with a wholesale value of nearly \$9 billion to 5.8 billion cases with a wholesale value of \$27.5 billion in 1990.

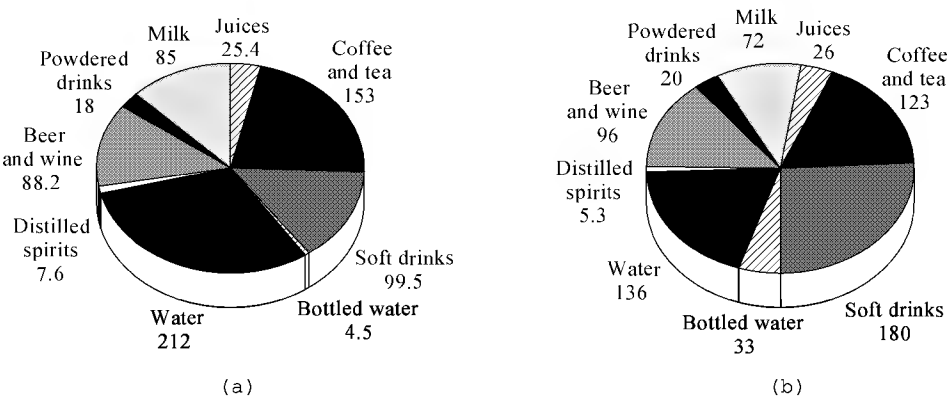


Fig. 1. Annual U.S. liquid consumption in liters per capita: (a) 1975, (b) 1990 (est) (1). To convert L to gal, divide by 3.785.

The soft drink industry is dominated by two key players, The Coca-Cola Company and Pepsico. These two companies produce eight of the ten top soft drink brands and comprise over 72% of the soft drink market in the United States (Figs. 2 and 3).

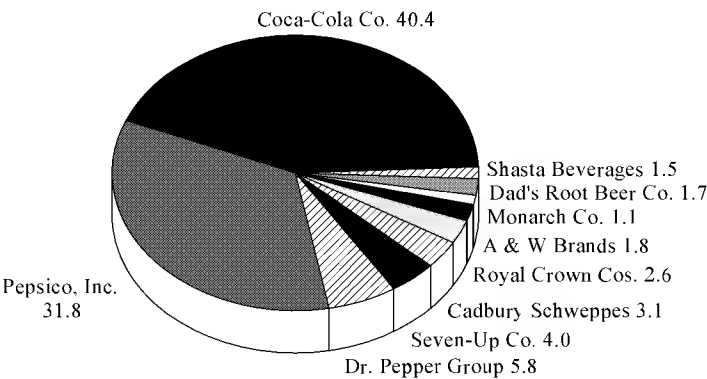


Fig. 2. Top ten U.S. soft drink franchisers in 1990 (est), % (2).

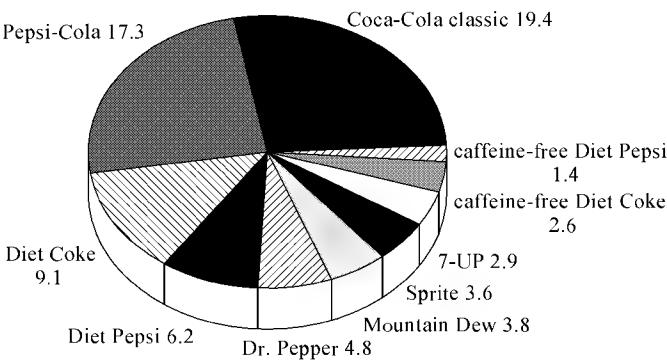


Fig. 3. Top ten U.S. soft drink brands in 1990 (est), % (2).

Colas represent the largest segment of the U.S. soft drink market followed by lemon–lime brands. Pepper-type, juice-based, root beer, and orange flavored soft drinks represent two to five percent of the total soft drink market (Fig. 4). Diet and caffeine-free categories represent the fastest growing segments of the market.

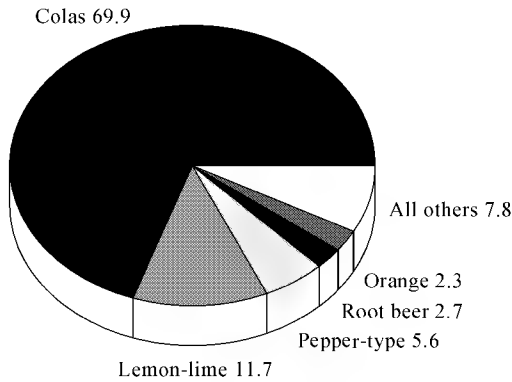


Fig. 4. Soft drink categories in 1990 (est), % (2).

Ingredients

Water. Water [7732-18-5] is the largest single ingredient used in carbonated beverages and must be of high purity. Drinking water supplied by local municipalities fails to meet the required purity levels for use in carbonated beverages. It must be treated to remove four types of contaminants that may affect the taste, odor, or appearance of the final beverage. The four contaminants are inorganic material, organic compounds, microbiological contamination, and particulate matter. The water treatment process employed in the soft drink industry varies but may include chemical treatment, reverse osmosis (qv), ultrafiltration (qv), and or ion exchange (qv) (see WATER, INDUSTRIAL WATER TREATMENT).

Chemical Treatment. Chemical treatment is used by most carbonated beverage facilities. Treatment includes chlorination for disinfection purposes and oxidation of some impurities in the water. The water is then softened through the addition of lime to reduce alkalinity by removing magnesium and calcium bicarbonates. The reaction products formed as a result of the softening process are removed by coagulation. The coagulants, ferrous sulfate or potassium aluminum sulfate, react with the calcium or magnesium hydroxides to form precipitates. The precipitates settle out and are removed from the bottom of the reaction tank. Any residual precipitates are removed by passing the water through a sand filter. Activated carbon adsorption is used to remove chlorine and any other organic compounds, thus reducing the chance of undesirable odors or tastes. The water may then go through a final polishing stage of filtration to remove any carbon fines.

Reverse Osmosis. This process can be used to remove most water contaminants. Water is pumped at high pressure through a semipermeable membrane. Particulate and microbiological contaminants are retained on the membrane because of pore size. Dissolved ions and organic material are affected by the charge on the membrane and are retained. The water that passes through the membrane can then be used for product water. Reverse osmosis is generally used as a polishing step for other water treating methods.

Ultrafiltration. This process removes macromolecules, microorganisms, particulate matter, and pyrogens using a thin, selectively permeable membrane. Ultrafiltration cannot remove ions from water and is generally employed as a polishing process.

Ion Exchange. Ion exchange, or demineralization, is used to remove inorganic materials from water. The process employs either a mixed bed of ion-exchange resins or separate beds of cation- and anion-exchange resins. A cation-exchange resin replaces cations, such as calcium, sodium, magnesium, or potassium, with hydrogen ions. The anion-exchange resin replaces anions, such as carbonates, bicarbonates, sulfates, and chlorides, with hydroxide ions. These resins can be regenerated and reused.

Sweeteners. The sweeteners (qv) used in carbonated beverages may be either nutritive or nonnutritive. The quality of the sweetener is one of the most important parameters affecting the overall quality of the beverage. Organoleptic profile (taste and odor), solubility, microbial stability, and temperature stability are important quality parameters.

Nutritive Sweeteners. These include granulated sucrose, sucrose in solution, invert sugar, dextrose, and high fructose corn syrup. Sucrose [57-50-1], C₁₂H₂₂O₁₁, obtained from cane or sugar beets, was historically used as the primary sweetener for carbonated beverages. In the presence of acids, sucrose is hydrolyzed to fructose [57-48-7], C₆H₁₂O₆, and dextrose (D-glucose) [50-99-7], C₆H₁₂O₆; the mixture is called invert sugar. The change in carbohydrate profile changes the perception of sweetness in the beverage. Some beverage manufacturers start with liquid invert sugar rather than allowing the beverage to invert over time.

High fructose corn syrup (HFCS) was first introduced to the beverage industry in the early 1970s. Improvements in quality encouraged parent soft drink companies to allow HFCS to replace sucrose as the primary nutritive sweetener for the beverage industry by 1984. HFCS is derived from corn starch through a process that includes breakdown of the starch to glucose, enzymatic conversion of glucose to fructose, separation of the sugars, and blending of the sugars to produce various concentrations of fructose and glucose. HFCS-42, HFCS-55, and HFCS-90 are available and contain varying concentrations of fructose and percent solids (Table 1). The choice of sweetener depends on the final sweetness desired and the particular beverage formulation.

Table 1. Nutritive Sweeteners Used in the Preparation of Carbonated Beverages

Type of sweetener	Sucrose, %	Polysaccharides, %	Dextrose, %	Fructose, %	Solids, %
liquid ^a sucrose	98–100	0	0	0	67
liquid ^a invert sugar	40–60	0	20–30	20–30	76
HFCS-42	0	2–9	49–53	40–44	71
HFCS-55	0	2–5	38–42	54–57	77
HFCS-90	0	1–2	7–8	89–91	77

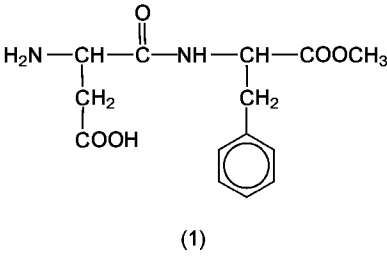
^a That is, aqueous solutions

Manufacturers may choose to use blends of nutritive sweeteners; the most common blends consist of various concentrations of liquid invert sugar and HFCS-42 or HFCS-55.

Nonnutritive Sweeteners. Diet or low calorie beverages represent a significant portion (27.7%) of the total soft drink market. The diet category is expected to increase at approximately 2% per year. Currently, saccharin and aspartame [22839-47-0], C₁₄H₁₈N₂O₅, are the only nonnutritive

sweeteners approved for use in beverages by the U.S. Food and Drug Administration (FDA). Saccharin [81-07-2], C₇H₅NO₃S, was first available for commercial use in 1900. It was used in soft drinks as a blend with sucrose during World War I because of the shortage of nutritive sweeteners. Saccharin is 300–400 times sweeter than sucrose. The FDA formally approved its use in foods and beverages in 1938. The FDA proposed a ban on saccharin as a bulk additive in foods in 1977. Congress has enforced and frequently renewed a moratorium on the proposed ban of saccharin in beverages.

Aspartame (1) is the primary nonnutritive sweetener used in carbonated soft drinks. It is approximately 200 times sweeter than sucrose. Aspartame is the methyl ester of a dipeptide of L-phenylalanine and L-aspartic acid.



Some sources consider aspartame a nutritive sweetener. It is sensitive to low pH and high temperatures and degrades over time. Aspartame can be used alone or in a blend with other sweeteners.

To meet consumer demands, manufacturers are developing new nonnutritive sweeteners that more closely match the taste and mouthfeel of sucrose. There are several nonnutritive sweeteners currently pending FDA approval for use in soft drinks. They include sucralose [56038-13-2], alitame [80863-62-3], encapsulated aspartame, cyclamates, and acesulfame-K [55589-62-3], also known as palitinit.

Acidulants. Acidulants give the beverage a tart or sour flavor, adjust pH to facilitate the function of benzoate as a preservative, reduce microbiological susceptibility, and act as a catalyst for the hydrolytic inversion process in sucrose sweetened beverages. The primary carbonated beverage acidulants are phosphoric acid [7664-38-2] and citric acid [77-92-9]. Other acidulants include ascorbic, tartaric, malic, and adipic acid (Table 2).

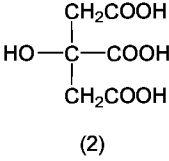
Table 2. Acids and Salts in Carbonated Beverages

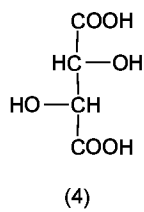
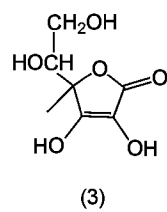
Name	CAS Registry Number	Molecular formula	Structure	Use
phosphoric acid	[7764-38-2]	H ₃ PO ₄	(HO) ₃ P=O	acidulant
citric acid	[77-92-9]	C ₆ H ₈ O ₇	(2)	acidulant
ascorbic acid ^a	[50-81-7]	C ₆ H ₈ O	(3)	antioxidant
2-tartaric acid	[87-69-4]	C ₄ H ₆ O	(4)	antioxidant nutrient
adipic acid	[124-04-9]	C ₁₀ H ₁₈ O ₄	HOOC(CH ₂) ₄ COOH	antioxidant
malic acid	[617-48-1]	C ₄ H ₆ O ₅		antioxidant
sodium benzoate	[532-32-1]	C ₇ H ₅ O ₂ Na		preservatives
potassium benzoate	[582-25-2]	C ₇ H ₅ O ₂ K		
sodium sorbate	[7757-81-5]	C ₆ H ₇ O ₂ Na	CH ₃ CH=CH—CH=CHCOO [−] Na ⁺	preservatives
potassium sorbate	[590-00-1]	C ₆ H ₇ O ₂ K	or CH ₃ CH=CH—CH=CHCOO [−] K ⁺	

^a Vitamin C.

Phosphoric Acid. This acid is the primary acidulant in cola beverages. Phosphoric acid is stronger than most organic acids and weaker than other mineral acids. The dibasic properties of phosphoric acid provide minor buffering capacity in the beverage. Food-grade phosphoric acid is commercially available in concentrations of 75°, 80°, and 85° and is one of the most economical acidulants.

Citric Acid. This acid is used in a variety of flavored carbonated beverages, including lemon–lime, orange, other fruit flavors, some root beers, and colas. Citric acid (2) is also a sequestering agent for heavy metals and can be used to some extent as an antioxidant. Citric acid (qv) is naturally found in most fruits and was originally obtained from lemons. It is commercially derived from the fermentation of dextrose and a strain of mold, *Aspergillus niger*. Citric acid can be added during the syrup manufacturing process as a powder or as a 50° solution.





Other Acids. Ascorbic acid (3) is used primarily as an antioxidant and to a lesser extent as an added nutrient in beverages. It oxidizes readily, preventing the oxidation of certain flavoring compounds. Tartaric (4) and adipic acids are used to a lesser extent in grape flavored beverages. Malic acid can be used as an alternative to citric acid in some fruit flavored beverages.

Preservatives. The carbonation and acid content in cola and lemon–lime beverages usually act as adequate preservation against microbial growth. Benzoate or sorbate salts are often added to other beverages for protection (Table 2).

Sodium or potassium benzoate at a concentration of 0.05% is a universally used preservative agent active against yeast and mold. At higher concentrations benzoate is also effective against bacteria. It is most effective at a pH between 2.0 and 4.0. Sodium or potassium sorbate inhibits the growth of yeast and mold and is most effective below pH 6.5.

Carbon Dioxide. Carbon dioxide [124-38-9] provides soft drinks with a pungent taste, acidic bite, and sparkling fizz. Carbon dioxide (qv) also acts as a preservative against yeast, mold, and bacteria. The carbon dioxide used in soft drinks must be food-grade and free of impurities that may affect the taste or odor of the final product.

Carbonation can be measured in terms of volumes of carbon dioxide dissolved in one liter of beverage at a standard temperature and pressure (0°C, 101.3 kPa = 1 atm). One liter of carbon dioxide dissolved in one liter of beverage has a carbonation volume of one.

Carbon dioxide gas is added to either the water used to prepare beverages or the syrup and water mixture, depending on the type of manufacturing equipment. In both manufacturing processes, the carbon dioxide gas is introduced under pressure to the system. The carbonation of the beverage is dependent on the carbon dioxide pressure and the temperature of the mixture.

Carbon dioxide concentrations vary depending on the beverage formulation. Cola and lemon–lime beverages normally contain more carbonation than berry flavored or other citrus beverages.

Flavors. Flavor is the most important attribute of a carbonated beverage. Most carbonated beverages contain complex mixtures of different flavors produced in several commercial forms as alcoholic solutions, emulsions, and concentrates. The majority of flavors used in carbonated beverages are derived from natural sources.

Caffeine. Caffeine [58-08-2], C₈H₁₀N₄O₂, is usually added to cola beverages for its pleasantly bitter taste. Cola beverages not containing caffeine are designated as caffeine-free.

Juice-Based Flavors. Fruit juices are concentrated for use in carbonated beverage flavors. The final juice is concentrated between four to six times its initial strength by removing the water under vacuum; it is then pasteurized. Orange, grapefruit, lemon, grape, and apple are the most common fruit juices used in carbonated beverages.

Essential Oils. Volatile oils from plants are referred to as essential oils. The oils can be obtained through steam distillation, solvent extraction, or separation of the oils from pressed fruit. They consist of oxygenated compounds, terpenes, and sesquiterpenes. The primary flavor components of essential oils are oxygenated compounds. Terpenes contain some flavors but are often removed from the essential oil because they are easily oxidized (causing off-flavors or odors) and are insoluble. Essential oils are prepared from fruits, herbs, roots, and spices.

Oleo Resins. These oily residues, obtained from the solvent extraction of herbs, contain more of the characteristic flavors than do the essential oils. The solvent extraction removes nearly all of the flavor bodies from the herb. The extract solvent is distilled, reducing the solution to an oily residue. Oleo resins of interest to the carbonated beverage industry are ginger, celery, and black pepper.

Alcoholic Solutions or Extracts. Alcoholic extracts are prepared by dissolving the flavor-bearing body in a solution of alcohol and water. They may require filtration using filter aids to remove any insoluble precipitates or oils that may form. Alcoholic extracts are clear solutions and are used in beverages that do not require a haze or cloudiness.

Emulsions. An emulsion is the mixture of essential oils with an emulsifying agent, such as gum acacia or tragacanth, that is then homogenized. The homogenization process reduces the size of the emulsion particle, increasing its stability. The specific gravity of the emulsion is altered using brominated vegetable oil or glyceryl abietate [1337-89-9] (ester gum) as weighting agents. The adjustment is necessary to keep the emulsion in proper suspension in the beverage. If the specific gravity of the emulsion is less than the finished beverage, it will float to the top, forming a neck ring. Emulsions always produce an initially cloudy beverage.

Concentrates. These are mixtures of alcoholic solutions or emulsions with other fruit juice mixtures to produce a water-soluble solution. The concentrate can be easily used in the manufacture of syrup, providing carbonated beverage of consistent quality.

Concentrated Flavor or Beverage Bases. Parent soft drink companies may provide franchise bottlers with concentrated flavor or beverage bases that contain all of the necessary ingredients with some exceptions. In certain cases, nutritive sweeteners, preservatives, and some nonnutritive sweeteners may be purchased by the franchise bottler or packaged separately.

Colorants. Colorants are used in beverages to provide additional sensory appeal. Carbonated beverage may contain some natural color from the use of natural flavors or juices but generally require additional colorants such as caramel or other artificial colors (see COLORANTS FOR FOOD, DRUGS, AND COSMETICS).

Caramel color is used in most cola and root beer flavored carbonated beverages. It is manufactured through the carefully controlled heat treatment of a good-grade carbohydrate source, usually dextrose, and a chemical catalyst, such as food-grade acids, bases, or salts. All caramels are colloidal in nature and carry a small ionic charge. Manufacturers of soft drinks may use caramels with different properties but most require a negatively charged caramel. Caramel is generally supplied in single- or double-strength formulations whose primary difference is the color intensity. The double-strength formulation is used in most diet or low calorie colas because it has a lower caloric contribution than single-strength formulations. A foaming caramel may be used in root beer formulations.

Five FDA approved artificial colors commonly used in soft drinks are listed in Table 3.

Table 3. Commonly Used Artificial Food Colors

FD & C designation	Common name	CAS Registry Number	CI name	CI number
Yellow #5	Tartrazine	[1934-21-0]	Food Yellow #4	19140

Yellow #6	Sunset Yellow FCF	[2783-94-0]	Food Yellow #3	15985
Red #40	Allura Red AC	[25956-17-6]	Food Red #17	16035
Green #3	Fast Green FCF	[2353-45-9]	Food Green #3	42053
Blue #1	Brilliant Blue FCF	[3844-45-9]	Food Blue #2	42090

The color is often added as a powder during the syrup manufacturing process either by itself or in a mixture with other dry ingredients. The color can also be mixed with the liquid flavor concentrate. All colors must be tested and released by the FDA.

Manufacturing

Carbonated beverages are manufactured by combining the concentrated flavorings (beverage bases) with a nutritive or nonnutritive sweetener and water to form a syrup; mixing the syrup with a proportioned quantity of carbonated water, filling and sealing the beverage in a container; and then packaging the container into a multipack secondary package (Fig. 5). This simplified process has remained relatively unchanged except for modernization and increased efficiency since the industry began.

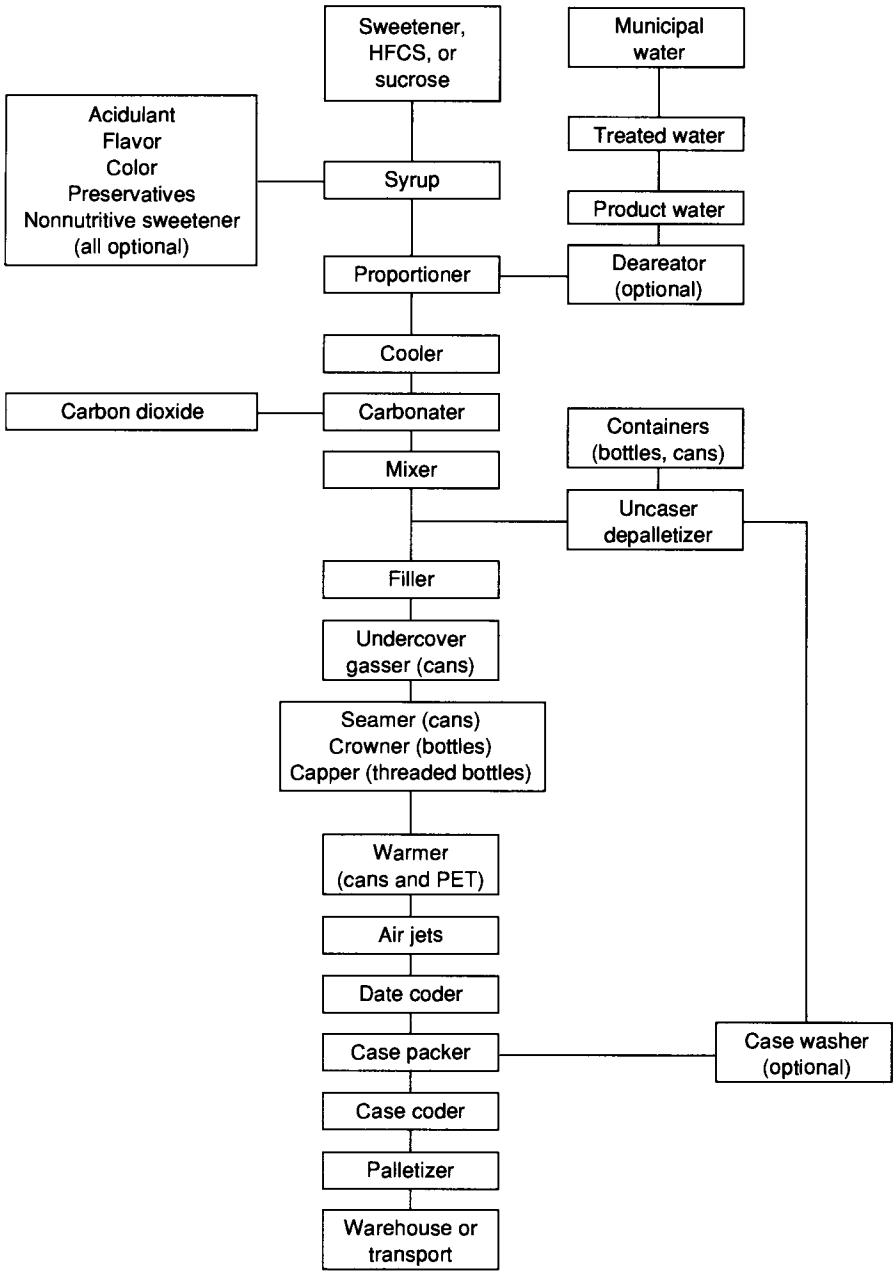


Fig. 5. Manufacturing process flow diagram.

Syrup Mixing and Handling. Most parent companies sell concentrated flavor bases to franchise bottlers and allow the bottlers to mix this with their own sweetener and water. This defrays shipping costs and reduces the labor demand on parent company manufacturing. In return, franchise bottlers are able to purchase sweeteners from local suppliers at a substantial discount and reduce their overall costs.

Concentrated flavor bases include all necessary flavors and ingredients with the exception of sweeteners and, in some cases, preservatives and acidulants. All of these components are mixed according to strict instructions to produce a quantity of syrup. A unit of syrup is defined by the parent company dependent on the brand but is often 189–3400 L (50 to 900 gallons).

A separate room is usually dedicated to syrup mixing. This room must be large enough to handle the various syrup batching requirements for efficient daily production and be of sanitary design to facilitate cleaning. Room design requires the floor to be made of an acid-resistant material such as quarry tile or have an epoxy coating. The walls may also be tiled or painted with an epoxy or latex paint to withstand the frequent cleaning demands.

Various sized tanks are required for the actual mixing. Additional tanks may be required for storage if large batches are made and held for any length of time. Tanks must be made of a corrosion-resistant stainless steel, such as 304 or 316, to prevent acidic syrups from picking up a metallic off-taste. Tanks also must have secured covers to prevent the entrance of airborne or other contaminants. Mixing tanks require agitators of sufficient size and speed to mix the viscous syrup within a reasonable time without harming the flavor by shearing or destroying the delicate flavor blends. Similarly, all pumps, valves, and lines must be of stainless steel or, in the case of lines, of an inert plastic material that does not impart an off-taste.

Once mixed, the syrup must be processed into the beverage as quickly as possible. Many soft drink brands contain delicate and sensitive flavors that may lose some of their taste characteristics because of acid hydrolysis or oxidation if kept in storage too long. Syrups made with aspartame must be processed quickly because this nonnutritive sweetener loses some of its sweetness over time in a low pH environment. Shelf lives of finished syrups depend greatly on their particular ingredients, their general flavor category (cola versus citrus), and whether their storage tanks are refrigerated. A refrigerated syrup retains its flavor longer.

Mixing Procedures. Each carbonated beverage flavor has its own unique mixing requirements but certain common principles apply. Preservatives such as sodium or potassium benzoate dissolve best in a nonacidic solution. Therefore, preservatives are usually dissolved in a mixing tank prior to the addition of flavors or acidulants. Conversely, aspartame dissolves best in an acidic solution and is usually added to a mixing tank after the flavors and acidulant have been added. A general mixing sequence is as follows:

- Add required treated water, withholding a quantity sufficient to rinse all containers to remove all traces of ingredients.
- Start agitator. Add preservatives if applicable, and mix until dissolved.
- Add nutritive sweetener if applicable.
- Add flavor concentrate, rinsing containers with water withheld for that purpose.
- Add aspartame if applicable.
- Add any remaining water to complete batch.
- Agitate until completely mixed (usually 30–90 min).
- Test syrup for quality control parameters, and release to production if analysis is satisfactory.

Filling. The filling process begins with mixing the syrup and treated water to beverage proportions and then carbonating this mixture. The water, and sometimes the finished beverage mixture, is often cooled to better facilitate carbonation and increase filling speed. Empty beverage containers are indexed at the filler after they have been washed, rinsed, or air blown, depending on the particular package. Containers are filled and then either crowned, capped, or in the case of cans, seamed to seal the container. From this point the filled container is transferred to packaging to be cased and palletized for distribution.

The filling process is relatively simple in design but can be complicated by the wide array of packages, products, container materials, and multiple secondary packaging options. For example, dozens of brands of soft drinks are manufactured by the same facility. Once canned, these brands can be loose-pack cased, six-pack cased, 12-pack wrapped, 15-pack wrapped, or 24-pack wrapped. The packaging decision is based on many factors including marketing strategy, promotions, and local market preferences.

Continuous Blend Production. The latest development in beverage manufacturing is the continuous blending of concentrate directly to beverage. This continuous blend system enjoys several advantages over the conventional syrup batch method in that finished syrup holding tanks are not required and the beverage is mixed immediately. Another advantage is that the total time required to produce the beverage is greatly reduced.

A continuous blend system requires predissolved powder components and sufficient liquid beverage base components. These are constantly metered and pumped into a beverage mixture. The components are mixed using positive displacement pumps that meter precise quantities. The continuous blend process requires the use of in-line ingredient monitors to measure the concentrations of ingredients constantly. Recent technological innovations have resulted in in-line monitors that are capable of measuring beverage components with the necessary precision required to produce a quality beverage.

Packaging

Carbonated beverages were packaged primarily in returnable glass bottles until 1948, representing 98.8% of the total take-home market. A few independent bottlers began using nonreturnable bottles in 1948, representing 0.2% of the market. By 1964 the nonrefillable bottlers represented 13% of the total take-home market.

Cans were introduced to the soft drink industry in the mid-1950s. By 1965, cans made up 6.5% of the soft drink market. Today cans are the largest selling package in the United States, exceeding 50% in many markets (Fig. 6).

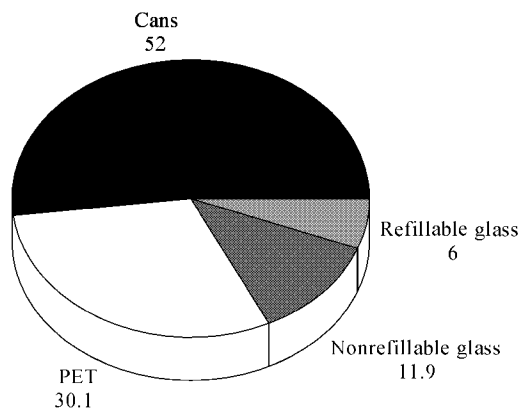


Fig. 6. U.S. soft drink packaging in 1990 (3).

Another significant development in the growth of soft drinks was the tremendous proliferation of packages starting in the mid-1950s. In 1953, The Coca-Cola Company abandoned its "one product and one package" philosophy relating to its 6.5-oz (0.2 L) bottle to compete with Pepsi-Cola's 12-oz bottle (0.35 L). Since that time, the types of packages have expanded to include dozens of sizes from 0.2 to 3 liters. Added to this wide array of sizes are the different container types including refillable glass, nonrefillable glass, poly(ethylene terephthalate) (PET) or plastic bottles, aluminum cans, steel cans, and even plastic (PET) cans. All of these options are offered to consumers to give the convenience and preference they desire. The increase in package sizes and options has been at least partially credited with increased sales volumes and per capita consumption for the last three decades.

Quality Control

Ingredients. Ingredients used in the manufacture of carbonated beverages must meet all *Food Chemical Codex* specifications and be approved for use in soft drinks by the FDA. In addition to the government stated specifications, manufacturers of carbonated beverages may complete additional analyses based on specific needs or concerns.

Drinking water supplied to carbonated soft drink manufacturing facilities from private or municipal sources must comply with all regulatory requirements. Treated water must meet all U.S. Environmental Protection Agency primary maximum contaminant levels and may also be subject to additional state requirements. Treated water is routinely analyzed for taste, odor, appearance, chlorine, alkalinity, iron, pH, total dissolved solids, hardness, and microbiological contamination.

Carbon dioxide used in carbonated beverages must be food-grade and must meet the Compressed Gas Association commodity specifications for carbon dioxide. In addition, carbon dioxide is tested for purity, taste, and odor before being used in the production of beverages.

Syrup. In typical manufacturing processes that produce syrup, several analytical parameters must be checked prior to packaging or beverage preparation. The sucrose or HFCS solids content is verified through the use of density meters or refractometers and reported as degree Brix, ° solids, Baumï, or g mL. The acidulant level is verified using titration or spectrophotometric methods. Preservative concentrations may be confirmed using high pressure liquid chromatography. Syrups are also evaluated for proper color, using spectrophotometric methods or colorimeters, and tested for microbial contamination.

Beverages. The quality control for carbonated beverages encompasses all aspects of the product from actual chemical components to the physical condition of the container. The beverage is evaluated using laboratory tests as well as in-line monitors.

Laboratory tests on the beverage include degree Brix, syrup to water ratio, taste, and microbiological testing. Beverages must first be decarbonated using blenders, air-stone degassing units, or ultrasonic baths before determining the degree Brix using density meters, hydrometers, or refractometers. The decarbonated beverage is then analyzed for acidulant content or ratio using titration or spectrophotometric methods.

Packaging. Incoming beverage packages are tested to ensure compliance with parent company specifications. Refillable bottles are visually inspected after washing to ensure that only clean and undamaged bottles are filled with beverage. In some refillable bottler operations, visual inspection is coupled with an electronic bottle inspection machine to further ensure the integrity of the bottles prior to filling. Packaged beverage is further tested for carbonation, closure application, fill height, and net contents. Beverage packages are usually tested at production start up and at various intervals of a production run as specified by the parent company.

Bottles of carbonated beverage are tested for carbonation using a Zahm-Nagel or Ashcroft carbonation tester. The carbonation can be calculated from the measured pressure and temperature values. Canned beverage is tested for carbonation and air content using a Zahm air tester.

Glass or plastic bottles that have plastic or aluminum closures are tested for removal torque. The removal torque represents the force required to remove the closure from the bottle. Closures are also evaluated to ensure that they have been properly applied and that they are tamper evident. Crown closures are also evaluated to ensure proper application.

Packaged carbonated beverage is tested for net contents or fill height to ensure that the package contains the stated weight or volume of beverage. The target value for each package should comply with individual state regulations.

Package Recycling

Because of the sheer volume of carbonated beverages consumed and the highly visible nature of the package, many consumers believe the soft drink containers make up a significant portion of the daily municipal waste. In reality, soft drink containers make up approximately 1.6° by weight of the total solid waste stream in the United States. This perception has led to several states enacting forced deposit legislation to reduce litter and encourage recycling.

The nine states that have enacted such laws were led by Oregon in 1972. Massachusetts and New York were the last two states to pass forced deposit legislation in 1983. Environmental groups and industry leaders continue to encourage other states to look beyond the narrow scope of regulating just beverage containers and to look at the entire solid waste issue.

Recycling and source reduction have been actively pursued by the carbonated beverage industry. In 1991, 64° of aluminum cans, 30° of PET bottles, and 30° of all carbonated beverage containers were recycled. Comprehensive recycling programs including curbside recycling collections have been initiated in 14° of the population (eight million homes). These programs were necessary to address the entire solid waste problem and not just a single element such as carbonated beverage containers.

Future Developments

The soft drink industry is changing rapidly. The industry enjoyed rapid growth and expansion in its early years with bottling plants numbering 7646 in 1930. However, the number of plants have been declining ever since. By 1982, the total number of bottling plants had dropped to 1700. The decline continues as bottlers consolidate and centralize production into larger facilities. The bulk of all soft drink production is now done by a few large bottlers. The large franchise companies control key portions of their bottling operations and therefore exert management influence with these bottlers. The trend is expected to continue with total soft drink production facilities numbering around 500 to 600 by 1995.

New packaging and packaging materials seem imminent. New nonnutritive sweeteners promise increased shelf life and improved taste for a calorie conscious society. Faster, more efficient production methods and equipment are being developed every day. Soft drink manufacturers will continue to expand markets overseas and attempt to increase per capital consumption in existing markets.

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CARBON DIOXIDE

Carbon dioxide [124-38-9], CO₂, is a colorless gas with a faintly pungent odor and acid taste first recognized in the sixteenth century as a distinct gas through its presence as a by-product of both charcoal combustion and fermentation. Today carbon dioxide is a by-product of many commercial processes: synthetic ammonia production, hydrogen production, substitute natural gas production, fermentation, limestone calcination, certain chemical syntheses involving carbon monoxide (qv), and reaction of sulfuric acid with dolomite. Generally present as one of a mixture of gases, carbon dioxide is separated, recovered, and prepared for commercial use as a solid (dry ice), liquid, or gas.

Carbon dioxide is also found in the products of combustion of all carbonaceous fuels, in naturally occurring gases, as a product of animal metabolism, and in small quantities, about 0.03 vol % , in the atmosphere. Its many applications include beverage carbonation, chemical manufacture, firefighting, food freezing, foundry-mold preparation, greenhouses, mining operations, oil well secondary recovery, rubber tumbling, therapeutical work, welding, and extraction processes. Although it is present in the atmosphere and the metabolic processes of animals and plants, carbon dioxide cannot be recovered economically from these sources.

Physical Properties

Some values of physical properties of CO₂ appear in Table 1. An excellent pressure–enthalpy diagram (a large Mollier diagram) over 260 to 773 K and 70–20,000 kPa (10–2,900 psi) is available (1). The thermodynamic properties of saturated carbon dioxide vapor and liquid from 178 to the critical point, 304 K, have been tabulated (2). Also given are data for superheated carbon dioxide vapor from 228 to 923 K at pressures from 7 to 7,000 kPa (1–1,000 psi). A graphical presentation of heat of formation, free energy of formation, heat of vaporization, surface tension, vapor pressure, liquid and vapor heat capacities, densities, viscosities, and thermal conductivities has been provided (3). Compressibility factors of carbon dioxide from 268 to 473 K and 1,400–69,000 kPa (203–10,000 psi) are available (4).

Table 1. Properties of Carbon Dioxide

Property	Value
sublimation point at 101.3 kPa ^a , °C	−78.5
triple point at 518 kPa ^b °C	56.5
critical temperature, °C	31.1
critical pressure, kPa ^b	7383
critical density, g /L	467
latent heat of vaporization, J /g ^c	
at the triple point	353.4
at 0°C	231.3
gas density at 273 K and 101.3 kPa ^a , g /L	1.976
liquid density	
at 273 K, g /L	928
at 298 K and 101.3 kPa ^a CO ₂ , vol %	0.712
viscosity at 298 K and 101.3 kPa ^a , mPa·s(cP)	0.015
heat of formation at 298 K, kJ /mol ^d	393.7

^a 101.3 kPa = 1 atm.
^b To convert kPa to psia, multiply by 0.145.
^c To convert J /g to Btu /lb, multiply by 0.4302.
^d To convert kJ /mol to Btu /mol, multiply by 0.9487.

Available data on the thermodynamic and transport properties of carbon dioxide have been reviewed and tables compiled giving specific volume, enthalpy, and entropy values for carbon dioxide at temperatures from 255 K to 1088 K and at pressures from atmospheric to 27,600 kPa (4,000 psia). Diagrams of compressibility factor, specific heat at constant pressure, specific heat at constant volume, specific heat ratio, velocity of sound in carbon dioxide, viscosity, and thermal conductivity have also been prepared (5).

Equations for viscosity at different temperatures, pressures, and thermal conductivity have also been provided (5). The vapor pressure function for carbon dioxide in terms of reduced temperatures and pressure is as follows:

log P_R = 4.2397 − 4.4229 / T_R − 5.3795 log T_R + 0.1832 (P_R / T_R²)

where P_R equals reduced pressure, which equals P / P_c (P_c critical pressure 7.38 MPa or 72.85 atm), and T_R equals reduced temperature, which equals T / T_c (T_c critical temperature, 304.2 K) (6). This equation gives accurate vapor pressure values from the triple point to the critical point. A table of reduced density values for carbon dioxide covering the range of reduced pressures from 0.3 to 500 kPa (0.044–72.5 psi) and reduced temperatures from 0.712 to 20 K is also supplied (6). Enthalpy values for carbon dioxide in the critical region, and with temperatures from 423 to 923 K and pressures from 0 to 20 MPa (0–200 atm), have been computed (7,8).

Diagrams of isobaric heat capacity (C_p) and thermal conductivity for carbon dioxide covering pressures from 0 to 13,800 kPa (0–2,000 psi) and 311 to 1088 K have been prepared. Viscosities at pressures of 100–10,000 kPa (1–100 atm) and temperatures from 311 to 1088 K have been plotted (9).

Vapor pressure data for solid carbon dioxide are given in Table 2 (10). The sublimation temperature of solid carbon dioxide, 194.5 K at 101 kPa (1 atm), was selected as one of the secondary fixed points for the International Temperature Scale of 1948.

Table 2. Vapor Pressure of Solid Carbon Dioxide^a

Temperature, °C	Pressure, Pa	Temperature, °C	Pressure, Pa
-188°C	1.333×10^{-4}	-148°C	1.333×10^1
-182°C	1.333×10^{-3}	-136°C	1.333×10^2
-175°C	1.333×10^{-2}	-120°C	1.333×10^3
-167°C	1.333×10^{-1}	-100°C	1.333×10^4
-159°C	1.333	-65°C	1.333×10^5

^a To convert Pa to mm Hg, divide by 1.333×10^2 .

The solubility of carbon dioxide in water is given in Figure 1 (11). Over the temperature range 273–393 K, the solubilities at pressures below 20 MPa (200 atm) decrease with increasing temperature. From 30 to 70 MPa (300–700 atm) a solubility minimum is observed between 343 and 353 K, with solubilities increasing as temperature increases to 393 K. Information on the solubility of carbon dioxide in pure water and synthetic seawater over the range 268 to 298 K and 101–4,500 kPa pressure (1–44 atm) is available (12,13).

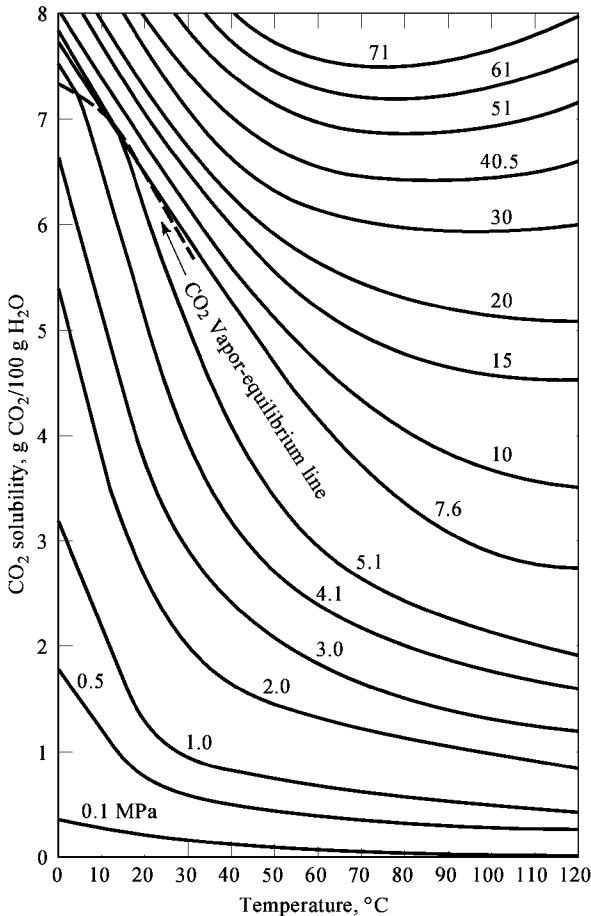
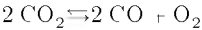


Fig. 1. Solubility of carbon dioxide in water at various pressures in MPa. To convert MPa to atm, multiply by 10.

The following tables of properties of carbon dioxide are available: enthalpy, entropy, and heat capacity at 0 and 5 MPa (0 and 50 atm, respectively) from 273 to 1273 K; pressure–volume product (PV), enthalpy, and isobaric heat capacity (C_p) from 373 to 1273 K at pressures from 5 to 140 MPa (50–1,400 atm) (14).
A more recent compilation includes tables giving temperature and PV as a function of entropies from 0.573 to 0.973 (zero entropy at 0°C, 101 kPa (1 atm) and pressures from 5 to 140 MPa (50–1400 atm) (15). Joule-Thomson coefficients, heat capacity differences ($C_p - C_v$), and isochoric heat capacities (C_v) are given for temperatures from 373 to 1273 K at pressures from 5 to 140 MPa.

Chemical Properties

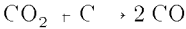
Carbon dioxide, the final oxidation product of carbon, is not very reactive at ordinary temperatures. However, in water solution it forms carbonic acid [463-79-6], H_2CO_3 , which forms salts and esters through the typical reactions of a weak acid. The first ionization constant is 3.5×10^{-7} at 291 K; the second is 4.4×10^{-11} at 298 K. The pH of saturated carbon dioxide solutions varies from 3.7 at 101 kPa (1 atm) to 3.2 at 2,370 kPa (23.4 atm). A solid hydrate [27592-78-5], $CO_2 \cdot 8H_2O$, separates from aqueous solutions of carbon dioxide that are chilled at elevated pressures.
Although carbon dioxide is very stable at ordinary temperatures, when it is heated above 1700°C the reaction forming CO proceeds to the right to an appreciable extent (15.8%) at 2500 K. This reaction also proceeds to the right to a limited extent in the presence of ultraviolet light and electrical discharges.



Carbon dioxide may be reduced by several means. The most common of these is the reaction with hydrogen.



This is the reverse of the water–gas shift reaction in the production of hydrogen and ammonia (qv). Carbon dioxide may also be reduced catalytically with various hydrocarbons and with carbon itself at elevated temperatures. The latter reaction occurs in almost all cases of combustion of carbonaceous fuels and is generally employed as a method of producing carbon monoxide.



Carbon dioxide reacts with ammonia as the first stage of urea manufacture to form ammonium carbamate [1111-78-0].



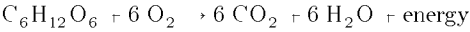
The ammonium carbamate then loses a molecule of water to produce urea [57-13-6], CO(NH₂)₂. Commercially, this is probably the most important reaction of carbon dioxide and it is used worldwide in the production of urea (qv) for synthetic fertilizers and plastics (see AMINO RESINS; CARBAMIC ACID).

Radioactive Carbon. In addition to the common stable carbon isotope of mass 12, traces of a radioactive carbon isotope of mass 14 with a half-life estimated at 5568 years are present in the atmosphere and in carbon compounds derived from atmospheric carbon dioxide. Formation of radioactive ¹⁴C is thought to be caused by cosmic irradiation of atmospheric nitrogen. The concentration of carbon-14 [14762-75-5] in atmospheric carbon dioxide is approximately constant throughout the world. The ratio of ¹⁴CO₂ [51-90-1] to ¹²CO₂ in the atmosphere, although constant for several hundred years, has decreased in the last sixty years by about 3‰ because of the influx of carbon dioxide in the atmosphere from the burning of fossil fuels, ie, coal, petroleum, and natural gas. Procedures have been developed for estimating the age of objects containing carbon or carbon compounds by determining the amount of radioactive ¹⁴C present in the material as compared with that present in carbon-containing substances of current botanical origin (16). Ages of materials up to 45,000 years have been estimated with the radiocarbon dating technique.

Carbon dioxide containing known amounts of ¹⁴C has been used as a tracer in studying botanical and biological problems involving carbon and carbon compounds and in organic chemistry to determine the course of various chemical reactions and rearrangements. It has also been used in testing gaseous diffusion theory with mixtures of CO₂ and ¹⁴CO₂ at elevated pressures (17).

Environmental Chemistry. Carbon dioxide plays a vital role in the earth's environment. It is a constituent in the atmosphere and, as such, is a necessary ingredient in the life cycle of animals and plants.

In animal metabolism, oxygen from the atmosphere reacts with sugars in the body to produce energy according to the overall formula:



The by-product CO₂ is released to the atmosphere. In plant metabolism, carbon dioxide from the air is taken into the leaves of the plant. Using energy from light, carbon dioxide reacts with water in the presence of enzymes to produce sugar. This reaction, photosynthesis, is the reverse of the above reaction.

The balance between animal and plant life cycles as affected by the solubility of carbon dioxide in the earth's water results in the carbon dioxide content in the atmosphere of about 0.03 vol % . However, carbon dioxide content of the atmosphere seems to be increasing as increased amounts of fossil fuels are burned. There is some evidence that the rate of release of carbon dioxide to the atmosphere may be greater than the earth's ability to assimilate it. Measurements from the U.S. Water Bureau show an increase of 1.36‰ in the CO₂ content of the atmosphere in a five-year period and predictions indicate that by the year 2000 the content may have increased by 25‰ (see AIR POLLUTION).

The effects of such an increase, if it occurs, are not known. It could result in a warmer temperature at the earth's surface by allowing the short heat waves from the sun to pass through the atmosphere while blocking larger waves that reflect back from the earth. If the earth's average temperature were to increase by several degrees, portions of the polar ice caps could melt causing an increase in the level of the oceans, or air circulation patterns could change, altering rain patterns to make deserts of farmland or vice versa.

On the other hand, it has been demonstrated that the addition of CO₂ to greenhouses increases the growth rate of plants so that an increase in the partial pressure of CO₂ in the air could stimulate plant growth making possible shorter growing seasons and increased consumption of carbon dioxide from the air. CO₂ is also used in water-treatment applications. Because it is significantly safer than mineral acids, it can be used to reduce the alkalinity of treated water.

Commercial Production

Sources of carbon dioxide for commercial carbon dioxide recovery plants are (1) synthetic ammonia and hydrogen plants in which methane or other hydrocarbons are converted to carbon dioxide and hydrogen (CH₄ + 2 H₂O → CO₂ + 4 H₂); (2) flue gases resulting from the combustion of carbonaceous fuels; (3) fermentation in which a sugar such as dextrose is converted to ethyl alcohol and carbon dioxide (C₆H₁₂O₆ → 2 C₂H₅OH + 2 CO₂); (4) lime-kiln operation in which carbonates are thermally decomposed (CaCO₃ → CaO + CO₂); (5) sodium phosphate manufacture (3 Na₂CO₃ + 2 H₃PO₄ → 2 Na₃PO₄ + 3 CO₂ + 3 H₂O); and (6) natural carbon dioxide gas wells.

Ammonia and Hydrogen Plants. More carbon dioxide is generated and recovered from ammonia and hydrogen plants than from any other source. Both plants produce hydrogen and carbon dioxide from the reaction between hydrocarbons and steam. In the case of hydrogen plants, the hydrogen is recovered as a pure gas. For ammonia plants the hydrogen is produced in the presence of air, controlled to give the volume ratio between hydrogen and nitrogen required to synthesize ammonia. In order to produce either product it is necessary to remove the carbon dioxide (18). The annual synthetic ammonia production capacity in the United States was about 16 × 10⁶ t in 1991 (see AMMONIA). For each ton of ammonia produced, more than a ton of carbon dioxide is generated. Hence the available carbon dioxide supply from this source is several times as large as the total commercial production of carbon dioxide. A substantial amount of the carbon dioxide recovered from ammonia plants is used for urea production.

Flue Gases. In a typical plant for producing gaseous carbon dioxide from coke, coal, fuel oil, or gas the fuel is burned under a standard water-tube boiler for the production of 1400–1800 kPa (200–260 psi) steam. At 613 K flue gases containing 10–18% carbon dioxide leave the boiler and pass through two packed towers where they are cooled and cleaned by water. The gases are then passed through a booster blower into the base of the absorption tower. The recovery system shown in Figure 2 is the Girbotol amine process (19) although an alkaline carbonate system may also be used (Fig. 2). In the tower, carbon dioxide is absorbed selectively by a solution of ethanolamines passing countercurrent to the gas stream (see ALKANOLAMINES). The carbon dioxide-free flue gases pass out of the top of the tower into the atmosphere, the carbon dioxide-bearing solution passes out from the bottom of the tower, through pumps and heat exchangers, into the top of a reactivation tower. Here heat strips the carbon dioxide from the amine solution and the reactivated solution returns through the heat-exchanger equipment to the absorption tower. Carbon dioxide and steam pass through the top of the reactivation tower into a gas cooler in which the steam condenses and returns to the tower as reflux. The carbon dioxide at this point is available as a gas at a pressure of about 200 kPa (2 atm). If liquid or solid carbon dioxide is desired it may be further purified for odor removal before compression.

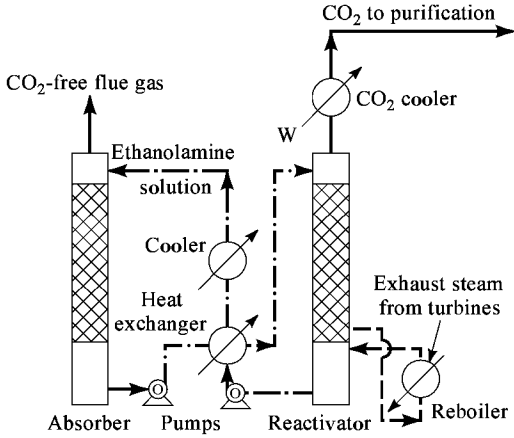


Fig. 2. Recovery of carbon dioxide using a Girbotol recovery unit.

The steam balance in the plant shown in Figure 2 enables all pumps and blowers to be turbine-driven by high pressure steam from the boiler. The low pressure exhaust system is used in the reboiler of the recovery system and the condensate returns to the boiler. Although there is generally some excess power capacity in the high pressure steam for driving other equipment, eg, compressors in the carbon dioxide liquefaction plant, all the steam produced by the boiler is condensed in the recovery system. This provides a well-balanced plant in which few external utilities are required and combustion conditions can be controlled to maintain efficient operation.

Fermentation Industry. Large quantities of carbon dioxide are present in gases given off in the fermentation of organic substances such as molasses, corn, wheat, and potatoes in the production of beer, distilled beverages, and industrial alcohol. These gases may contain impurities such as aldehydes, acids, higher alcohols, glycerol, furfural, glycols, and hydrogen sulfide. Two processes are in general use for removing these contaminants and preparing the carbon dioxide for use. In one process, this is accomplished by the use of activated-carbon adsorbents; the other process is a chemical purification process (see BEER; BEVERAGE SPIRITS, DISTILLED; ETHANOL; FERMENTATION). A very small percentage of commercial CO₂ is produced by this process.

The Backus process (20,21) uses active carbon. Carbon dioxide gases from the top of the fermentors are collected in a low pressure gas holder to even out the flow. Roots-Connorsville-type blowers force the gases through Feld scrubbers where they are washed with water to remove the bulk of entrained material, alcohols, aldehydes, etc. The washed gases pass through active-carbon purifiers, which adsorb the balance of impurities, and then to the compressors. The adsorption process gives off heat, which is removed by water coils embedded in the carbon. Periodically, the carbon beds must be reactivated to remove accumulated impurities. This is accomplished by passing live steam through the carbon bed and water coils. After steaming, the carbon beds are dried by passing air through them; they are then ready for reuse. In general, two sets of active-carbon purifiers are used, one on-stream and the other being reactivated (see ADSORPTION, GAS SEPARATION).

The Reich process (22,23) uses chemical processes to remove impurities. Carbon dioxide from the fermentors is bubbled through a wash box, or catchall, which removes entrained liquids and mash. The gases pass through three packed scrubbing towers. In the first, dilute alcohol solution is passed countercurrent to the gases for de-alcoholizing the gases. The other two towers use water for further removal of alcohol. The alcohol is returned to the alcohol plant for distillation or use in the fermentors. The washed gas passes through a gas holder and blower, which boosts it through the balance of the purification plant. The first stage in this section is a potassium dichromate washer for the oxidation of organic impurities and the removal of hydrogen sulfide. Next, the gas is passed countercurrent to concentrated sulfuric acid for dehydration and dichromate removal. Entrained sulfuric acid is removed by a dry solid ash tower and the residual oxidized material is removed by countercurrent scrubbing with a light oil. The gas is then ready for compression. In some installations the first stage of compression is inserted before the dichromate washer and the purification operations are carried out at 600–800 kPa (87–116 psi).

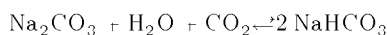
Lime-Kiln Operation. Gases containing up to 40% carbon dioxide from the lime kiln pass through a cyclone separator, which removes the bulk of entrained dust. The gas is then blown through the two scrubbers, which remove the finer dust, cooled, and passes into an absorption tower. Here carbon dioxide may be recovered by the sodium carbonate or Girbotol process.

Sodium Phosphate Manufacturing. Some pure carbon dioxide gas is available as a by-product in plants manufacturing sodium phosphate from sodium carbonate [497-19-8] and phosphoric acid [7664-38-2]. Two carbon dioxide plants were installed prior to 1962 to utilize this by-product gas.

Natural Gas Wells. Natural gas, containing high percentages of carbon dioxide, has been found in a number of locations including New Mexico, Colorado, Utah, and Washington. Several small plants have been in operation for a number of years producing commercial solid and liquid carbon dioxide from these sources (see GAS, NATURAL). Several large CO₂ plants are in operation using well gas as a source of CO₂.

There are a number of methods of recovering carbon dioxide from industrial or natural gases. The potassium carbonate and ethanolamine processes are most common. In all these processes the carbon dioxide-bearing gases are passed countercurrent to a solution that removes the carbon dioxide by absorption and retains it until it is desorbed in separate equipment. All of these processes are in commercial use and the most suitable choice for a given application depends on individual conditions. Water could be used as the absorbing medium, but this is uncommon because of the relatively low solubility of carbon dioxide in water at normally encountered pressures. The higher solubility in the alkali carbonate and ethanolamine solutions is the result of a chemical combination of the carbon dioxide with the absorbing medium.

Sodium Carbonate Process. This process of recovering pure carbon dioxide from gas containing other diluents, such as nitrogen and carbon monoxide, is based on the reversibility of the following reaction:



This reaction proceeds to the right at low temperatures and takes place in the absorber where the carbon dioxide-bearing gases are passed countercurrent to the carbonate solution. The amount of carbon dioxide absorbed in the solution varies with temperature, pressure, partial pressure of carbon dioxide in the gas, and solution strength. Operating data on this reaction have been obtained by numerous investigators (24). The reaction proceeds to the left when heat is applied. The reaction takes place in a lye boiler. A heat exchanger preheats the strong lye approaching the boiler and cools the weak lye returning to the absorber. A lye cooler further cools weak lye to permit the reaction to proceed further to the right in the absorber. The carbon dioxide gas and water vapor released from the solution in the boiler pass through a steam condenser where the water condenses and returns to the system. The cool carbon dioxide proceeds to the gas holder and compressors. The absorber is generally a carbon-steel tower filled with coke, Raschig rings, or steel turnings. The weak solution is distributed evenly over the top of the bed and contacts the gas on the way down. Some plants operate with the tower full of sodium carbonate solution and allow the gas to bubble up through the liquid. Although this may afford a better gas-to-liquid contact, an appreciable amount of power is required to force the gas through the tower.

The lye boiler is usually steam heated but may be direct-fired. Separation efficiency may be increased by adding a tower section with bubble-cap trays. To permit the bicarbonate content of the solution to build up, many plants are designed to recirculate the lye over the absorber tower with only 20–25% of the solution flowing over this tower passing through the boiler. Several absorbers may also be used in series to increase absorption efficiencies.

The sodium carbonate process is used in a number of dry-ice plants in the United States, although its operating efficiency is generally not as high as that of processes using other solutions. These plants obtain the carbon dioxide from flue gases as well as lime-kiln gases.

Potassium Carbonate Process. The potassium carbonate process is similar to the sodium carbonate process. However, as potassium bicarbonate [298-14-6] is more soluble than the corresponding sodium salt, this process permits a more efficient absorption than the other. The equipment layout is the same and the operation technique is similar.

There are several variations of the potassium carbonate process. The hot potassium carbonate process does not involve cooling of the solution flowing from the boiler to the absorber (25). Absorption takes place at essentially the same temperature as solution regeneration. In its simplest form this process uses an absorption column, a regeneration column, a heated boiler or reboiler, and a circulating pump. This arrangement minimizes energy requirements and capital costs but the higher absorbing temperature does not allow the carbon dioxide removal to be as complete as with lower temperatures. One modification that improves removal is the use of a split stream flow to the absorber. Part of the solution is cooled and used at the top of the absorber. The balance of the solution, uncooled, is added part way down the absorber. The combined solution from the absorber then flows to the regenerator. In another modification two-stage absorption and regeneration is used. The carbonate solution from the absorber flows to the regeneration column. Part of the solution is withdrawn from the column at some intermediate point and pumped, uncooled, to an intermediate point in the absorber. The remaining solution undergoes a more complete regeneration and is cooled and pumped to the top of the absorber.

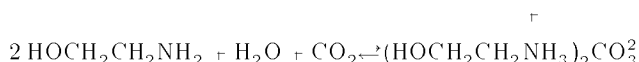
Three commercial processes that use these various hot carbonate flow arrangements are the promoted Benfield process, the Catacarb process, and the Giammarco-Vetrocoke process (26–29). Each uses an additive described as a promoter, activator, or catalyst, which increases the rates of absorption and desorption, improves removal efficiency, and reduces the energy requirement. The processes also use corrosion inhibitors, which allow use of carbon-steel equipment. The Benfield and Catacarb processes do not specify additives. Vetrocoke uses boric acid, glycine, or arsenic trioxide, which is the most effective.

These processes have been used in many plants to remove carbon dioxide from ammonia synthesis gas or natural gas. They are most effective if the

gas stream being treated is at elevated pressures (1700 kPa (17 atm) or higher). This increases the carbon dioxide partial pressure so that the hot potassium carbonate solution absorbs a substantial amount of carbon dioxide. The stripping tower or regenerator operates at or near atmospheric pressure.

Ethanolamines may also be added to carbonate solutions to improve their performance (30). Vapor pressure-equilibrium data for the K_2CO_3 – $KHCO_3$ – CO_2 – H_2O system are given (31).

Girbotol Amine Process. This process developed by the Girdler Corporation is similar in operation to the alkali carbonate processes. However, it uses aqueous solutions of an ethanolamine, ie, either mono-, di-, or triethanolamine. The operation of the Girbotol process depends on the reversible nature of the reaction of CO_2 with monoethanolamine [141-43-5] to form monoethanolamine carbonate [21829-52-7].



The reaction proceeds in general to the right at low temperatures (300–338 K) and absorbs the carbon dioxide from the gas in the absorber as shown in Figure 2. The amine solution, rich in carbon dioxide, passes from the bottom of the tower through a heat exchanger, where it is preheated by hot, lean solution returning from the reactivator. On passing into the reactivator the solution passes countercurrent to a stream of carbon dioxide and steam, which strips the carbon dioxide out of the solution. By the time the solution reaches the bottom of the tower, where heat is supplied by a steam-heated or direct-fired reboiler, it has been reactivated. This hot solution (373–423 K) passes out of the tower, through the heat exchanger and cooler, and returns to the absorber tower.

The amine process or one of the various carbonate processes is used in the majority of CO_2 -removal applications. At low pressures the amine process has clear advantages in removal efficiency and installed cost. At higher pressures the increased carbon dioxide partial pressures favor a higher CO_2 content in the absorbing solution, whether carbonate or amine, which permits a lower steam usage per unit of carbon dioxide stripped from the absorbent. Until recently, amine systems have not been able to take full advantage of the benefits of higher absorber pressure because of corrosion problems. The CO_2 -rich amine solution is inherently more corrosive than potassium carbonate solutions so that the stronger the amine solution and the greater the carbon dioxide content the worse the corrosion potential. To hold corrosion to a minimum, amine solution designs have been limited to a maximum solution strength of 20 wt% with a maximum CO_2 content of about 0.0374 m³ L (5 ft³ gal) of solution. Even then, some plants experience severe corrosion problems requiring replacement of some carbon-steel equipment with stainless steel. Carbonate solutions pick up more CO_2 per unit of solution than the amines, resulting in a lower circulation rate and a correspondingly lower heat regeneration requirement.

Overall comparison between amine and carbonate at elevated pressures shows that the amine usually removes carbon dioxide to a lower concentration at a lower capital cost but requires more maintenance and heat. The impact of the higher heat requirement depends on the individual situation. In many applications, heat used for regeneration is from low temperature process gas, suitable only for boiler feed water heating or low pressure steam generation, and it may not be useful in the overall plant heat balance.

Union Carbide has developed Amine Guard, which essentially eliminates corrosion in amine systems (32–35). It permits the use of substantially higher amine concentrations and greater carbon dioxide pick-up rates without corrosive attack. This results in an energy requirement comparable to that of the carbonate process and allows the use of smaller equipment for a specific CO_2 -removal application thereby reducing the capital cost.

Solubility of carbon dioxide in ethanolamines is affected by temperature, amine solution strength, and carbon dioxide partial pressure. Information on the performance of amines is available in the literature and from amine manufacturers. Values for the solubility of carbon dioxide and hydrogen sulfide mixtures in monoethanolamine and for the solubility of carbon dioxide in diethanolamine are given (36,37). Solubility of carbon dioxide in monoethanolamine is provided (38). The effects of catalysts have been studied to improve the activity of amines and provide absorption data for carbon dioxide in both mono- and diethanolamine solutions with and without sodium arsenite as a catalyst (39). Absorption kinetics over a range of contact times for carbon dioxide in monoethanolamine have also been investigated (40).

Sulfinol Process. The Sulfinol process was developed during the 1960s to remove carbon dioxide and other acidic gas from gas streams at high partial pressures. It uses a circulating solution with a flow pattern similar to those in the amine and carbonate processes. Regeneration occurs at low pressure, and heat is exchanged between the regenerated solution and the solution from the absorber. The Sulfinol solution is a mixture of sulfolane [126-33-0] (tetrahydrothiophene 1,1-dioxide), an alkanolamine, and water.

The process is capable of achieving higher solubilities of CO_2 in the solution without the corrosion problems encountered with amine systems before the advent of Amine Guard. The Sulfinol process is used in over 50 plants worldwide; nevertheless, it is used less often than the amine or carbonate processes.

Rectisol Process. This is one of several processes that use a solvent for removing carbon dioxide from gas streams. In the Rectisol process, the solvent is usually methanol and the operating temperature of the absorber is about 273 K. The process uses an absorption column and stripping column with intermediate pumps and heat exchangers. It is necessary to cool the process gas to the absorbing temperature. Split flow of the solvent stream to the absorber is used, with partially stripped solvent from the midsection of the stripper being used at the top of the absorber. Stripping is accomplished by pressure release, heat, and contact with an inert stripping gas, which is blown through the column.

The processes using physical absorption require a solvent circulation proportional to the quantity of process gas, inversely proportional to the pressure, and nearly independent of the carbon dioxide concentration. Therefore, high pressures could favor the use of these processes. The Rectisol process requires a refrigeration system and more equipment than the other processes. This process is primarily used in coal gasification for simultaneous removal of H_2S , COS, and CO_2 .

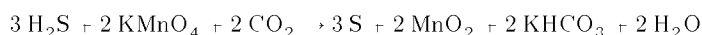
Purisol Process. This is a solvent process which uses *N*-methyl-2-pyrrolidinone [872-50-4] as the solvent and benefits from high pressure, 7000 kPa (69 atm) or higher. All commercial installations are at pressures above 4000 kPa (39 atm).

Fluor Process. This is a solvent process that uses propylene carbonate [108-32-7]. Propylene carbonate has a high solubility for CO_2 , a low solubility for other light gases, is chemically stable, and noncorrosive to carbon steel. Physical solvent plants represent a higher capital cost than the carbonate or amine process plants but may result in reducing operating costs where high pressures are involved. Seven plants using the Fluor process for removal of acidic gases were in existence by 1970; five natural gas plants, one hydrogen, and one ammonia plant.

Pressure Swing Adsorption. A number of processes based on Pressure Swing Adsorption (PSA) technology have been used in the production of carbon dioxide. In one version of the PSA process, CO_2 is separated from CH_4 using a multibed adsorption process (41). In this process both CH_4 and CO_2 are produced. The process requires the use of five adsorber vessels. Processes of this type can be used for producing CO_2 from natural gas wells, landfill gas, or from oil wells undergoing CO_2 flooding for enhanced oil recovery (see ADSORPTION, GAS SEPARATION).

Methods of Purification. Although carbon dioxide produced and recovered by the methods outlined above has a high purity, it may contain traces of hydrogen sulfide and sulfur dioxide, which cause a slight odor or taste. The fermentation gas recovery processes include a purification stage, but carbon dioxide recovered by other methods must be further purified before it is acceptable for beverage, dry ice, or other uses. The most commonly used purification methods are treatments with potassium permanganate, potassium dichromate, or active carbon.

Potassium Permanganate. Probably the most widely used process for removing traces of hydrogen sulfide from carbon dioxide is to scrub the gas with an aqueous solution saturated with potassium permanganate [7722-64-7]. Sodium carbonate is added to the solution as buffer. The reaction is as follows:

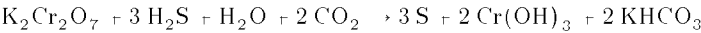


The precipitated manganese dioxide and sulfur are discarded. The solution is used until it becomes spent or so low in potassium permanganate that it is no longer effective and is discarded and replaced. It is customary to place two scrubbers in series, with the liquid flow countercurrent to the gas flow, to more efficiently use the permanganate solution. When the solution in the first scrubber is spent, with respect to the gas, the positions of the scrubbers are

reversed and the spent scrubber is recharged with fresh solution.

Two types of scrubbers are used. The simpler consists of a vessel half or two-thirds full of solution. The gas feeds into the bottom of the vessel and bubbles up through the solution. The other scrubber is a small packed tower through which the gas stream is passed countercurrent to a recirculating shower of potassium permanganate and soda ash solution. The latter requires a circulating pump and a solution mix chamber, but has the advantage of reducing the pressure drop through the equipment to a minimum. The solution is used until spent and then discarded. Two scrubbers of this type may also be used to improve efficiency.

Potassium Dichromate. This method is similar in application to the potassium permanganate method.



The precipitated chromic hydroxide and sulfur are discarded. This process is used to purify carbon dioxide from fermentation in the Reich process and as a final cleanup after the alkali carbonate or ethanolamine recovery processes (22,23).

Active Carbon. The process of adsorbing impurities from carbon dioxide on active carbon or charcoal has been described in connection with the Backus process of purifying carbon dioxide from fermentation processes. Space velocity and reactivation cycle vary with each application. The use of active carbon need not be limited to the fermentation industries but, where hydrogen sulfide is the only impurity to be removed, the latter two processes are usually employed (see CARBON, ACTIVATED CARBON).

Methods of Liquefaction and Solidification. Carbon dioxide may be liquefied at any temperature between its triple point (216.6 K) and its critical point (304 K) by compressing it to the corresponding liquefaction pressure, and removing the heat of condensation. There are two liquefaction processes. In the first, the carbon dioxide is liquefied near the critical temperature; water is used for cooling. This process requires compression of the carbon dioxide gas to pressures of about 7600 kPa (75 atm). The gas from the final compression stage is cooled to about 305 K and then filtered to remove water and entrained lubricating oil. The filtered carbon dioxide gas is then liquefied in a water-cooled condenser.

The second liquefaction process is carried out at temperatures from 261 to 296 K, with liquefaction pressures of about 1600–2400 kPa (16–24 atm). The compressed gas is precooled to 277 to 300 K, water and entrained oil are separated, and the gas is then dehydrated in an activated alumina, bauxite, or silica gel drier, and flows to a refrigerant-cooled condenser (see DRYING AGENTS). The liquid is then distilled in a stripper column to remove noncombustible impurities. Liquid carbon dioxide is stored and transported at ambient temperature in cylinders containing up to 22.7 kg. Larger quantities are stored in refrigerated insulated tanks maintained at 255 K and 2070 kPa (20 atm), and transported in insulated tank trucks and tank rail cars.

Solidification. Liquid carbon dioxide from a cylinder may be converted to "snow" by allowing the liquid to expand to atmospheric pressure. This simple process is used only where very small amounts of solid carbon dioxide are required because less than one-half of the liquid is recovered as solid.

Solid carbon dioxide is produced in blocks by hydraulic presses. Standard presses produce blocks 25 × 25 × 25 cm, 50 × 25 × 25 cm, or 50 × 50 × 25 cm. A 25-cm cube of dry ice weighs 23 kg, allowing for about 10% sublimation loss during storage and shipment (some 27-kg blocks are also produced). Dry ice is about 1.7 times as dense as water ice, whereas its net refrigerating effect on a weight basis is twice that of water ice. Automation and improved operating cycles have increased dry-ice press capacities so that one 50 × 50 × 30 cm press can produce more than thirty metric tons of dry-ice blocks per day (42).

Liquid carbon dioxide from a supply tank at 700 kPa (7 atm) and 227 K is fed to the press chamber through an automatic feed valve. The pressure in the press is maintained slightly above the triple point (480–550 kPa or 70–80 psi). The quantity fed to the press may be controlled by a timer, or a device that measures the level of liquid in the press chamber. The pressure is reduced and the evolved CO₂ vapor is returned to a recycle system. When the pressure falls below the triple point (518 kPa or 75 psi), the liquid CO₂ solidifies to form carbon dioxide snow. Heat-exchange units are used to cool the liquid CO₂ with cold vapors from the press. About 50% of the liquid fed to the press remains as snow when the pressure has dropped close to atmospheric. The hydraulic rams then press the snow to a solid block of dry ice. The block moves along a conveyor and is cut by band saws into four blocks, which are subsequently carried through automatic weighing and packaging machines.

Carbon dioxide is ordinarily dehydrated during the liquefaction cycle to prevent freeze-ups in the condenser and flow valves in the liquid lines. In some cases brittle or crumbly blocks of dry ice have been formed. This difficulty has been overcome either by varying the residual moisture content of the liquid carbon dioxide, or by injecting minute quantities of colorless mineral oil or diethylene glycol into the liquid carbon dioxide entering the press. If the dry ice is to be used for edible purposes, the additive must meet FDA specifications.

Although liquid carbon dioxide may be stored without loss in tanks and cylinders, dry ice undergoes continuous loss in storage because of sublimation. This loss can be minimized by keeping the dry ice in insulated boxes or bins. Special insulated rail cars and trucks are used for hauling dry-ice blocks. Most plants produce the material at the time it is sold to avoid storage losses and rehandling costs.

Economic Aspects

Carbon dioxide production is presented in Table 3. Throughout the 1970s and 1980s production increased steadily at a rate of 15 to 20% per year. The chief reason for this large predicted increase is the rapid increase in the amount of carbon dioxide used for secondary oil recovery. Table 3 indicates peak use of solid carbon dioxide in 1985 but actually dry-ice production has declined steadily over the last twenty years with the only increases occurring between 1984 and 1985. Liquid carbon dioxide production grew at an annual rate of 5.6% during the 1984–1989 period (43).

Table 3. Carbon Dioxide Production in the United States, 10³ t

Year	Total	Solid	Liquid and gas
1971	1219	287	932
1975	1679	319	1360
1980	2833	313	2520
1985	8031	413	7618
1987	7620	309	7311

Much more carbon dioxide is generated daily than is recovered (44). The decision whether or not to recover by-product carbon dioxide often depends on the distance and cost of transportation between the carbon dioxide producer and consumer. For example, it has become profitable to recover more and more carbon dioxide from CO₂-rich natural gas wells in Texas as the use of carbon dioxide in secondary oil recovery has increased. The production levels for enhanced oil recovery are generally not reported because of the captive nature of the application.

Toxicity

Although carbon dioxide is a constituent of exhaled air, high concentrations are hazardous. Up to 0.5 vol % carbon dioxide in air is not considered harmful, but carbon dioxide concentrates in low spots because it is one and one-half times as heavy as air. Five vol % carbon dioxide in air causes a threefold increase in breathing rate and prolonged exposure to concentrations higher than 5% may cause unconsciousness and death. Ventilation sufficient to prevent accumulation of dangerous percentages of carbon dioxide must be provided where carbon dioxide gas has been released or dry ice has been used for cooling.

Uses

A large portion of the carbon dioxide recovered is used at or near the location where it is generated as an ingredient in a further processing step. In this case, the gaseous form is most often used. Low temperature liquid and solid carbon dioxide are used for refrigeration. Where the producer and the consumer are distant, carbon dioxide may be liquified to reduce transportation cost and revaporized at the point of consumption.

About 51° of the carbon dioxide consumed in the United States is used in the food industry. It is generally purchased in liquid form but may be used in any form. It is generally used for food freezing or chilling. Numerous patents on applications and equipment for these applications have been received.

Approximately 18° of carbon dioxide output is used for beverage carbonation. Both soft drinks and beer production consume the largest quantity of CO₂ for carbonation (see CARBONATED BEVERAGES).

About 10° of the carbon dioxide produced is for chemical manufacturing. Sold as a liquid, it is used as a raw material, for inerting and pressurizing, and for cooling. Other applications include metal working (4° o) and oil and gas recovery (6° o).

Dry Ice. Refrigeration of foodstuffs, especially ice cream, meat products, and frozen foods, is the principal use for solid carbon dioxide. Dry ice is especially useful for chilling ice cream products because it can be easily sawed into thin slabs and leaves no liquid residue upon evaporation. Crushed dry ice may be mixed directly with other products without contaminating them and is widely used in the processing of substances that must be kept cold. Dry ice is mixed with molded substances that must be kept cold. For example, dry ice is mixed with molded rubber articles in a tumbling drum to chill them sufficiently so that the thin flash or rind becomes brittle and breaks off. It is also used to chill golf-ball centers before winding.

Dry ice is used to chill aluminum rivets. These harden rapidly at room temperature, but remain soft if kept cold with dry ice. It has found numerous uses in laboratories, hospitals, and airplanes as a convenient and readily available low temperature coolant.

Liquid Carbon Dioxide. The rapid increase in the use of liquid carbon dioxide is the result of new applications as well as improved facilities for transporting, storing, and handling liquid carbon dioxide. Carbon dioxide manufacturers have developed refrigerated bulk-liquid storage systems that they install and maintain for large consumers. These systems are available in sizes from 2 to 50 tons and have an insulated storage tank, maintained at 2080 kPa (20.5 atm) and 255 K by a Freon refrigeration unit, with a refrigeration coil in the upper part of the storage tank. An external vaporizer is provided when gaseous carbon dioxide is needed. Liquid-level and pressure relief valves, and a safety rupture disk, are provided. The entire assembly is enclosed in a sheet-steel housing mounted on a steel base, and requires nominal power. A 12-ton unit is supplied with a 1500-W (two-horsepower) refrigeration unit. Vaporizers can be heated by electricity or steam. One kg of steam vaporizes approximately 6 kg of CO₂. The storage tanks are refilled by the CO₂ supplier, either by tank truck or rail car delivery.

Ready availability and easy application of bulk liquid carbon dioxide have caused it to replace dry ice in many cases. Liquid CO₂ can be stored without loss and is easily measured or weighed. Liquid carbon dioxide is also used, along with dry ice, for direct injection into chemical reaction systems to control temperature.

Liquid carbon dioxide provides the most readily available method of rapid refrigeration and is used for rapid chilling of loaded trucks and rail cars before shipment. A two to four minute injection of liquid carbon dioxide into a loaded ice cream truck causes the temperature to drop as much as 70°C, flushing the warm air out of the truck and leaving a layer of carbon dioxide snow in the truck, which sublimates slowly to provide additional refrigeration. This greatly reduces the load on the truck's mechanical refrigeration system and eliminates the time lag in cooling the truck contents to a safe storage temperature. Test chambers for environmental studies have been effectively cooled at temperatures to 80°C with liquid carbon dioxide, either by direct injection, or by using the liquid to chill circulating refrigerant liquids. The speed with which chilling may be obtained and the low equipment cost required have been the main factors in the selection of liquid carbon dioxide for this service.

Liquid carbon dioxide has been used for many years in the Long-Airdox blasting system for mining coal. A steel cartridge containing liquid carbon dioxide is placed in a hole drilled in the coal seam. A heating mixture in the cartridge is ignited electrically. This vaporizes the carbon dioxide, causing the pressure to increase enough to burst a steel rupture disk and release the carbon dioxide, which shatters the coal. The cartridge is then recovered and reused.

Liquid carbon dioxide is used as a source of power in certain applications. The vapor pressure of liquid carbon dioxide (7290 kPa or 72 atm at 294 K) may be used for operating remote signaling devices, spray painting, and gas-operated firearms. Carbon dioxide in small cylinders is also used for inflating life rafts and jackets.

Fire-extinguishing equipment, ranging from hand-type extinguishers to permanent installations in warehouses, chemical plants, ships, and airplanes, uses liquid carbon dioxide. In addition to its snuffing action liquid carbon dioxide exerts a pronounced cooling effect helpful in fire extinguishing. It may be used on all types of fires and leaves no residue, but care must be exercised to safeguard against suffocation of personnel.

Carbon dioxide is sometimes added to irrigation water, in the same manner as fertilizer ammonia, in hard water regions. Carbon dioxide is also used with other gases in treating respiratory problems and in anesthesia.

In addition to chemical synthesis and enhanced oil recovery, gaseous carbon dioxide is used in the carbonated beverage industry. Carbon dioxide gas under pressure is introduced into rubber and plastic mixes, and on pressure release a foamed product is produced. Carbon dioxide and inert gas mixtures rich in carbon dioxide are used to purge and fill industrial equipment to prevent the formation of explosive gas mixtures.

The addition of small amounts of carbon dioxide to the atmosphere in greenhouses greatly improves the growth rate of vegetables and flowers.

Carbon dioxide is widely used in the hardening of sand cores and molds in foundries. Sand is mixed with a sodium silicate binder to form the core or mold after which it is contacted with gaseous carbon dioxide. Carbon dioxide reacts with the sodium silicate to produce sodium carbonate and bicarbonate, plus silicic acid, resulting in hardening of the core or mold without baking.

The use of carbon dioxide gas for shielded arc welding with semiautomatic microwire welding equipment has led to welding speeds up to 10 times those obtainable within conventional equipment. No cleaning or wire brushing of the welds is required (45) (see WELDING).

Carbon dioxide gas is used to immobilize animals prior to slaughtering them (46). In addition to providing a humane slaughtering technique, this results in better quality meat. The CO₂ increases the animal's blood pressure, thereby increasing blood recovery. The increased accuracy obtainable in the killing operation reduces meat losses because of cut shoulders.

As a weak acid (in aqueous solution) carbon dioxide neutralizes excess caustic in textile manufacturing operations. It does not injure fabrics and is easy to use. Carbon dioxide is also used for neutralizing alkaline wastewaters, treating skins in tanning operations, and carbonating treated water to prevent scaling.

Carbon dioxide is used as a chemical reagent in the manufacture of sodium salicylate, basic lead carbonate or white lead, and sodium, potassium, and ammonium carbonates and bicarbonates.

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CARBON DISULFIDE

Carbon disulfide [75-15-0] (carbon bisulfide, dithiocarbonic anhydride), CS₂, is a toxic, dense liquid of high volatility and flammability. It is an important industrial chemical and its properties are well established. Low concentrations of carbon disulfide naturally discharge into the atmosphere from certain soils, and carbon disulfide has been detected in mustard oil, volcanic gases, and crude petroleum. Carbon disulfide is an unintentional by-product of many combustion and high temperature industrial processes where sulfur compounds are present.

Carbon disulfide was first prepared nearly two hundred years ago by heating sulfur with charcoal. That general approach was the only commercial route to carbon disulfide until processes for reaction of sulfur and methane or other hydrocarbons appeared in the 1950s. Significant commercial production of carbon disulfide began around 1880, primarily for agricultural and solvent applications. Both the physical and chemical properties of carbon disulfide are utilized in industry. Commercial uses grew rapidly from about 1929 to 1970, when the principal applications included manufacturing viscose rayon fibers, cellophane, carbon tetrachloride, flotation aids, rubber vulcanization accelerators, fungicides, and pesticides. Production of carbon disulfide in the United States has declined in recent years. Other chemical fibers and films, as well as environmental and toxicity considerations related to carbon tetrachloride, have had significant impact on the demand for carbon disulfide. Worldwide annual production capacity in 1991 was approximately 1.3 million tons, with actual production estimated at about one million metric tons.

Physical Properties

Pure carbon disulfide is a clear, colorless liquid with a delicate etherlike odor. A faint yellow color slowly develops upon exposure to sunlight. Low-grade commercial carbon disulfide may display some color and may have a strong, foul odor because of sulfurous impurities. Carbon disulfide is slightly miscible with water, but it is a good solvent for many organic compounds. Thermodynamic constants (1), vapor pressure (1,2), spectral transmission (3,4), and other properties (1,2,5–7) of carbon disulfide have been determined. Principal properties are listed in Table 1.

Table 1. Properties of Carbon Disulfide

Property	Values			References
<i>General</i>				
melting point, K		161.11		5
latent heat of fusion, kJ kg ^a		57.7		5
boiling point at 101.3 kPa ^b , °C		46.25		2
flash point at 101.3 kPa ^b , °C		30		8
ignition temperature in air, °C				2
10-s lag time		120		
0.5-s lag time		156		
critical temperature, °C		273		2
critical pressure, kPa ^b		7700		2
critical density, kg m ³		378		2
solubility H ₂ O in CS ₂				9
at 10°C, ppm		86		
at 25°C, ppm		142		
dielectric constant		2.641		10
<i>Liquid at temperature</i> , °C	0°C	20°C	46.25°C	
density, kg m ³	1293	1263	1224	2
specific heat, J (kg·K) ^a	984	1005	1030	2
latent heat of vaporization, kJ kg ^a	377	368	355	1
surface tension, mN M (dyn cm)	35.3	32.3	28.5	2
thermal conductivity, W (m·K)		0.161		2
viscosity, mPa·s(cP)	0.429	0.367	0.305	2
refractive index, n _D	1.6436	1.6276		11
solubility in water, g kg soln	2.42	2.10	0.48	2
vapor pressure, kPa ^b	16.97	39.66	101.33	2
<i>Gas at temperature</i> , °C ^c	46.25	200	400°C	
density, kg m ³	2.97	1.96	1.37	1
specific heat, J (kg·K) ^{a,d}	611	679	730	6
viscosity, mPa·s(cP)	0.0111	0.0164	0.0234	7
thermal conductivity, W (m·K)	0.0073			7
<i>Thermochemical data at 298 K^a</i>				
heat capacity, C _p ⁰ , J (mol·K) ^a		45.48		12
entropy, S ⁰ , J (mol·K) ^a		237.8		12
heat of formation, H _f ⁰ , kJ mol ^a		117.1		12
free energy of formation, G _f ⁰ , kJ mol ^a		66.9		12

^a To convert J to cal, divide by 4.184.
^b To convert kPa to atm, divide by 101.3
^c At absolute pressure, 101.3 kPa.
^d C_p - C_v = 1.21 at 100°C (2).

Carbon disulfide is completely miscible with many hydrocarbons, alcohols, and chlorinated hydrocarbons (9,13). Phosphorus (14) and sulfur are very soluble in carbon disulfide. Sulfur reaches a maximum solubility of 63% S at the 60°C atmospheric boiling point of the solution (15). Solubility data for carbon disulfide in liquid sulfur at a CS₂ partial pressure of 101 kPa (1 atm) and a phase diagram for the sulfur–carbon disulfide system have been published (16). Vapor–liquid equilibrium and freezing point data are available for several binary mixtures containing carbon disulfide (9).

Under extremely high pressures of about 5.5 GPa (5.4 × 10⁴ atm) and temperatures up to 175°C, a black, solid form of carbon disulfide has been observed (17).

Chemical Properties

The low flash point temperature of −30°C at atmospheric pressure and wide flammability range of carbon disulfide deserve special attention (18). The flash point is lowered if the pressure is decreased or the oxygen content enriched. The flammability limits or explosive ranges depend on conditions of temperature, pressure, and geometry of the enclosure. Flammability limits of 1.06–50.0 vol % carbon disulfide in air are reported for upward propagation and 1.91–35.0 vol % for downward propagation in a 75-mm diameter glass tube (19). The upper flammability limit can be significantly decreased by dilution with carbon dioxide (20). Maximum explosive force occurs at a 4–8% concentration of carbon disulfide in air, at which a maximum absolute pressure increase of 730 kPa (7.2 atm) has been measured (21).

Hot surfaces and electric sparks are potential ignition sources for carbon disulfide. The ignition temperature depends on specific conditions, and values from 90 to 120°C in air have been reported (2,22). Data on carbon disulfide oxidation and combustion have been summarized (18). Oxidation products are generally sulfur dioxide [7446-09-5] and carbon dioxide [124-38-9]:



Carbonyl sulfide and carbon monoxide [630-08-0] can also form under certain conditions.

Thermodynamic calculations for reactions forming carbon disulfide from the elements are complicated by the existence of several known molecular species of sulfur vapor (23,24). Thermochemical data have been reported (12). Although carbon disulfide is thermodynamically unstable at room temperature, the equilibrium constant of formation increases with temperature and reaches a maximum corresponding to 91% conversion to carbon disulfide at about 700°C. Carbon disulfide decomposes extremely slowly at room temperature in the absence of oxidizing agents.

Carbon disulfide chemistry is thoroughly described in several publications, which include many references (15,25–28). Several important reactions are mentioned here.

Carbon disulfide is essentially unreactive with water at room temperature, but above about 150°C in the vapor phase some reaction occurs forming carbonyl sulfide (carbon oxysulfide) [463-58-1] and hydrogen sulfide [7783-06-4]. Carbonyl sulfide is an intermediate in the hydrolysis reaction:

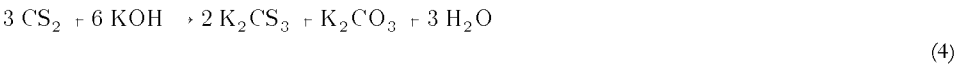


At temperatures of 300–600°C in the presence of an activated alumina catalyst, carbon dioxide and hydrogen sulfide are formed in almost quantitative yields (29):



This is a desirable side reaction in the first catalytic reactor of the Claus sulfur recovery process.

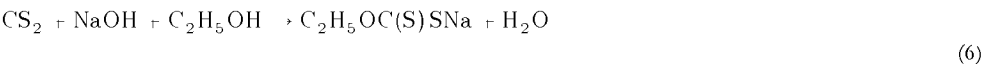
Carbon disulfide slowly reacts with alkali hydroxides to form trithiocarbonates and alkali carbonates:



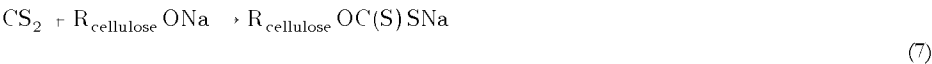
Trithiocarbonates can also be prepared from aqueous alkali sulfides:



Industrially important dithiocarbonates (xanthates) result from reaction with various alcoholic alkalies:



Of great commercial significance is preparation of sodium cellulose xanthate [9032-37-5] solution (viscose) by reaction with alkali cellulose:



Cellulose is subsequently regenerated from the viscose solution in sulfuric acid and carbon disulfide is liberated. These are the basic steps in manufacturing viscose rayon. The production of regenerated cellulose is estimated to account for more than 75% of the total carbon disulfide consumption worldwide (see FIBERS, REGENERATED CELLULOSICS).

Carbon disulfide and chlorine react in the presence of iron catalysts to give carbon tetrachloride [56-23-5] and sulfur monochloride [10025-67-9]:



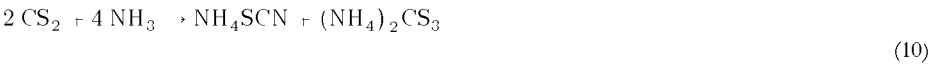
This is followed by a second reaction where sulfur monochloride becomes the chlorinating agent:



Reactions 8 and 9 have been used in the large-scale production of carbon tetrachloride since the early 1900s. As a result of decreased demand for carbon tetrachloride, this process is no longer used in the United States (see CHLOROCARBONS AND CHLOROHYDROCARBONS, CARBON TETRACHLORIDE).

If bromine is used in equation 8, carbon tetrabromide [558-13-4] is formed. With a minor amount of iodine present, and in the absence of iron catalyst, carbon disulfide and chlorine react to form trichloromethanesulfonyl chloride (perchloromethyl mercaptan [594-42-3]), CCl₃SCl, which can be reduced with stannous chloride or tin, and hydrochloric acid to form thiophosgene (thiocarbonyl chloride [463-71-8], CSCl₂, an intermediate in the synthesis of many organic compounds (see SULFUR COMPOUNDS).

Carbon disulfide reacts with concentrated ammonia to give ammonium thiocyanate [1762-95-4] and ammonium trithiocarbonate [13453-08-2] in a reaction promoted by alumina catalysts:



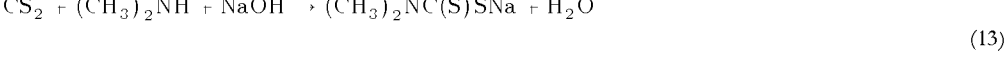
At approximately 160°C, some of the ammonium thiocyanate is converted to thiourea [62-56-6], H₂NCSNH₂, in low yield. With alcoholic ammonia, ammonium dithiocarbamate [513-74-6] forms:



Carbon disulfide reacts with primary and secondary amines to yield substituted ammonium salts of N-substituted dithiocarbamic acids, RNHC(S)SNH₃R and R₂NC(S)SNH₂R₂:

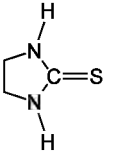


Industrially important alkali salts result if alkali hydroxide is present, such as the reaction with dimethylamine [124-40-3] forming sodium dimethyl dithiocarbamate [128-04-1]:

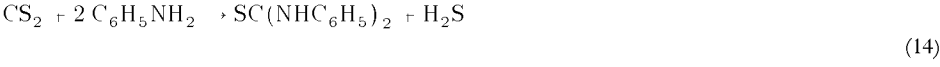


Analogous reactions form sodium methyldithiocarbamate [137-42-8] from methylamine, and disodium ethylenebis(dithiocarbamate) [142-59-6] from ethylenediamine. Iron, manganese, and zinc salts can be prepared from the sodium salts; heavy metals form characteristically colored compounds with dithiocarbamates.

Ethylenediamine reacts with carbon disulfide in alcoholic solution to give ethylenethiourea (2-imidazolidinethione [96-45-7]).



In boiling excess aniline, thiocarbamilide (1,3-diphenyl-2-thiourea [102-08-9]) is formed:



If sulfur is present, another industrially important compound results, 2-mercaptobenzothiazole (2-benzothiazolethiol [149-30-4]).

Carbonyl sulfide is a coproduct of many carbon disulfide oxidation reactions. Some examples are



With alkyl mercuric hydroxide:



Carbon disulfide reacts with Grignard reagents to prepare the corresponding dithiocarboxylic acids:



For example, dithiobenzoic acid [121-68-6] results from the reaction of carbon disulfide, phenyl bromide, ether, and magnesium.

Sodium azidodithiocarbonate [38093-88-8] is prepared by the reaction of aqueous sodium azide [26628-22-8] at 40–50°C:



Sodium azidodithiocarbonate decomposes with evolution of nitrogen gas on addition of iodine, thus providing a useful qualitative test for the presence of residual carbon disulfide in aqueous solutions (25).

Carbon disulfide reacts with alkanols or dialkyl ethers at 250–500°C over activated alumina catalyst to give dialkyl sulfides. For example, methanol yields dimethyl sulfide [75-18-3].

Hydrogen reduces carbon disulfide at high temperatures by the following reactions:



Hydrogenation at lower temperature and in the presence of catalysts yields organic sulfur compounds. With a reduced nickel catalyst at 180°C, methanedithiol [6725-64-0] is formed:



With a cobalt catalyst at 250°C, methanethiol (methyl mercaptan [74-93-1]) results:



Dimethyl sulfide [75-18-3], thioethers, thioformaldehyde [865-36-1], and thiophene [110-02-1] are among other possible carbon disulfide hydrogenation

products.

Manufacture

The earliest method for manufacturing carbon disulfide involved synthesis from the elements by reaction of sulfur and carbon as hardwood charcoal in externally heated retorts. Safety concerns, short lives of the retorts, and low production capacities led to the development of an electric furnace process, also based on reaction of sulfur and charcoal. The commercial use of hydrocarbons as the source of carbon was developed in the 1950s, and it was still the predominate process worldwide in 1991. That route, using methane and sulfur as the feedstock, provides high capacity in an economical, continuous unit. Retort and electric furnace processes are still used in locations where methane is unavailable or where small plants are economically viable, for example in certain parts of Africa, China, India, Russia, Eastern Europe, South America, and the Middle East. Other technologies for synthesis of carbon disulfide have been advocated, but none has reached commercial significance.

Charcoal–Sulfur Process. Sulfur vapor reacts with charcoal at temperatures of 750–900°C to form carbon disulfide:



Sulfur vapor is an equilibrium mixture of several molecular species, including S₈, S₂, and S₂[−]. The equilibrium shifts toward S₂ at higher temperatures and lower pressures. The overall reaction is endothermic and theoretically consumes 1950 kJ/kg (466 kcal/kg) of carbon disulfide when the reactants are at 25°C and the products are at 750°C. Most of the heat input goes into dissociation of sulfur vapor to the reactive species, S₂. Equation 25 is slightly exothermic when the reactants are at a constant temperature of 750°C.

Charcoal–sulfur processes need low ash hardwood charcoal, prepared at 400–500°C under controlled conditions. At the carbon disulfide plant site, the charcoal is calcined before use to expel water and residual hydrogen and oxygen compounds. This precalcination step minimizes the undesirable formation of hydrogen sulfide and carbonyl sulfide. Although wood charcoal is preferred, other sources of carbon can be used including coal (30,31), lignite chars (32,33), and coke (34). Sulfur specifications are also important; low ash content is necessary to minimize fouling of the process equipment.

Various reactor designs have been proposed, including fluidized beds (35–37), a whirlpool-type system (38), and a moving refractory bed to superheat the sulfur (39).

Retort Process. Retorts for producing carbon disulfide are typically oval or cylindrical vessels approximately 1 m in diameter by 3 m high, constructed from chrome alloy steel or cast iron (40,41). Normally one to four retorts are installed in a single furnace, fired with coal, gas, or oil. Alternatively, external electric heaters can be used. The precalcined charcoal is intermittently charged to the top of the retort through a special valve arrangement. Sulfur is added continuously near the bottom of the retort. The sulfur may be first vaporized and superheated to about 700°C in a pipe-coil heat exchanger located in the furnace. Carbon disulfide forms as the sulfur vapor rises through the hot charcoal at 850–900°C. Carbon disulfide, excess sulfur, and other vapors exit from the top of the retort through a duct. Nonreactive ash consolidates with charcoal dust and sifts down to the bottom of the retort from where the residue is periodically removed. Depending on the quality of the raw materials, deposits on the inside walls of the retort must be scraped off approximately monthly. Retorts must be replaced every 1–2 years due primarily to corrosive attack from sulfur vapor. Production capacities are typically up to about 5 tons of carbon disulfide per day per retort with external sulfur vaporization, or 1–3 tons per day with liquid sulfur feed.

The vapor leaving the retort consists of carbon disulfide along with smaller amounts of free sulfur, hydrogen sulfide, and carbonyl sulfide. Sulfur is condensed and recycled. Carbon disulfide is next condensed and then distilled to yield a pure product. In some adaptations, gases leaving the primary condensation are treated by mineral oil absorption to remove residual carbon disulfide selectively, which is later recovered by stripping. The distilled carbon disulfide is treated with lime or dilute sodium hydroxide to neutralize any remaining hydrogen sulfide or other acidic impurities, and the product is finally washed with water. Depending on local circumstances, the tail gas, containing principally hydrogen sulfide, is either flared, incinerated, treated with caustic soda solution to make coproduct sodium hydrogen sulfide [16721-80-5], NaSH, or sent to a Claus sulfur recovery unit. Raw material and energy usages per kg of carbon disulfide product are approximately 0.92–0.95 kg sulfur, 0.22–0.25 kg charcoal, and 8.4–10.0 MJ (2000–2400 kcal) fuel.

Electric Furnace Process. In this process charcoal and sulfur continuously react in a resistance-type electric furnace (40,42–44). One such furnace described in the literature is a cylindrical, refractory-lined vessel roughly 5 m in diameter by 10 m high. Lump charcoal is fed at the top through a gas-lock valve. Electric current supplied to two or four electrodes in the base of the furnace generates heat in passing through the bed of charcoal between opposing electrodes. The electrodes may either be radially or axially placed in the cylindrical furnace. Liquid sulfur enters the furnace at multiple locations in the sidewall near the base, where it quickly vaporizes and heats to 800–1000°C. Carbon disulfide forms in the lower section of the furnace. As the vapors rise, heat is transferred to incoming charcoal in the upper section. Product purification is by methods similar to those used in the retort process, except that entrained dust is normally removed from the vapor prior to the sulfur condensation step. Because heat is formed internally instead of being conducted through a thick wall, large-capacity reactors are feasible. Vessels can last many years, depending largely on the integrity of the lining. Sulfur and charcoal usages are similar to those of the retort process. Electric power consumption is approximately 4.0–4.8 MJ (1.1–1.3 kWh) per kg of carbon disulfide, about half the external energy required for the retort process. Electric furnaces were first employed for carbon disulfide around 1900 but did not gain wide acceptance until the 1940s.

Hydrocarbon–Sulfur Process. The principal commercial hydrocarbon is methane from natural gas, although ethane, and olefins such as propylene (45,46), have also been used.

Methane [74-82-8] reacts with sulfur essentially without side reactions:



At 400–700°C, equilibrium exceeds 99.9% (24). About 5–10% excess sulfur is usually maintained in the reaction mixture to promote high methane conversion and to minimize by-product yield. Carbon disulfide is also formed by the following reaction that is 80% complete at equilibrium at 700°C (47):



Reaction 27 is usually negligible in practice because of the less favorable equilibrium and the usual presence of excess sulfur, which favors reaction 26.

Other hydrocarbons can be used. Stoichiometrically, ethane [74-84-0] is preferable to methane since its lower hydrogen/carbon ratio results in a smaller yield of coproduct hydrogen sulfide:



Propane [74-98-6] and heavier paraffins tend to form undesired products, although reaction conditions can be controlled to minimize coke formation (48).

Propylene [115-07-1] can be used in a properly designed system (45,46):



Extensive research has been conducted on catalysts that promote the methane–sulfur reaction to carbon disulfide. Data are published for silica gel (49), alumina-based materials (50–59), magnesia (60,61), charcoal (62), various metal compounds (63,64), and metal salts, oxides, or sulfides (65–71). For a silica gel catalyst the rate constant for temperatures of 500–700°C and various space velocities is (72)

$$\log k_c = 10.9 - 131.4 / [2.303(RT)]$$



Side reactions reduce the yield (99). Proposed processes for obtaining carbon disulfide from hydrogen sulfide and methane include a high temperature plasma (100) and low temperature operation with a catalyst and oxygen (101).

Hydrogen sulfide and carbon react at 900°C to give a 70% yield of carbon disulfide (102,103). A process for reaction of coke and hydrogen sulfide or sulfur in an electric-resistance-heated fluidized bed has been demonstrated on a laboratory scale (104). Hydrogen sulfide also forms carbon disulfide in reactions with carbon monoxide at 600–1125°C (105) or carbon dioxide at 350–450°C in the presence of catalysts (106).

Sulfur dioxide [7446-09-5] and methane react to form carbon disulfide in a yield of 84% at 850°C in the presence of certain catalysts (107). Sulfur dioxide and anthracite at 900–1000°C produce very high yields (108).

Carbonyl sulfide can be either a starting or intermediate material (108–110), or it can be used as a fluidizing gas in a carbon fluid-bed process (111). Making carbon disulfide from boiler flue gas by catalytically reducing SO₂ with CO to COS, and then converting COS to CS₂ over an alumina catalyst has been proposed (112).

Handling, Shipment, and Storage

Transportation of carbon disulfide is controlled by federal regulations (113). Acceptable shipping containers include drums, tank trucks, special portable tanks, and rail tank cars. Barges have been used in the past. The United States Department of Transportation classifies carbon disulfide as a flammable liquid and a poison. For ship transport, carbon disulfide must be marked as a marine pollutant (114). All air transport, cargo, or passenger, is forbidden (115).

Carbon disulfide is normally stored and handled in mild steel equipment. Tanks and pipes are usually made from steel. Valves are typically cast-steel bodies with chrome steel trim. Lead is sometimes used, particularly for pressure relief disks. Copper and copper alloys are attacked by carbon disulfide and must be avoided. Carbon disulfide liquid and vapor become very corrosive to iron and steel at temperatures above about 250°C. High chromium stainless steels, glass, and ceramics may be suitable at elevated temperatures.

Contact of carbon disulfide with air should be avoided because the combination of high volatility, wide flammability range, and low ignition temperature results in a readily combustible mixture (116). Carbon disulfide must be stored in inert-blanketed, closed tanks. Normally carbon disulfide is transferred from vessels or tank cars through a downpipe by displacement with an inert material such as water or nitrogen (8,117). Direct pumping requires special equipment and precautions, hence that method of transfer is less common. Carbon disulfide is normally padded with water in storage tanks and bulk containers. Nitrogen blanketing has been used in cold climates. A combination of water with nitrogen above it can also be used, but in any case the total space not occupied by liquid carbon disulfide must be filled with inert material. The tanks themselves should be underwater or surrounded by dikes capable of holding the total tank contents. All equipment containing carbon disulfide should be located well away from potential sources of ignition, which include open flames, frictional heat, sparks, exposed electric light bulbs, and bare steam pipes. Good ground or floor-level ventilation should be provided because carbon disulfide vapor is heavier than air and can accumulate in low areas. Each piece of stationary equipment should be individually grounded by easily-visible conductors. Automatic monitoring of grounding continuity, with electrical detection and alarms, is recommended. Temporary grounding connections should be provided for movable equipment, such as drums or tank cars. Drums should be kept in a shaded but ventilated area with provision for cooling by water spray or other means if temperature exceeds ca 30°C. All of the equipment and operations preferably should be outdoors.

Small carbon disulfide fires can be smothered with carbon dioxide. Large fires can be controlled with certain types of foams or by a fog or spray of water with attention to proper impoundment of the contaminated water runoff. Without containment, the runoff may transport toxic fumes and fire or explosion hazards to other areas, such as sewers. Caution should be used in fighting a carbon disulfide fire because the flame is nearly invisible and a product of combustion is toxic sulfur dioxide. Special fire-fighting procedures have been published (118,119). Guidelines for emergency response to leaks, spills, and fires are available from the Department of Transportation (120). Cleanup of spills or disposal of wastes containing carbon disulfide must be managed in accordance with government regulations (22,121,122).

Economic Aspects

Depending on energy and raw material costs, the minimum economic carbon disulfide plant size is generally in the range of about 2000–5000 tons per year for an electric furnace process and 15,000–20,000 tons per year for a hydrocarbon-based process. A typical charcoal–sulfur facility produces approximately 5000 tons per year. Hydrocarbon–sulfur plants tend be on the scale of 50,000–200,000 tons per year. It is estimated that 53 carbon disulfide plants existed throughout the world in 1991 as shown in Table 2. The production capacities of known hydrocarbon–sulfur based plants are listed in Table 3. The United States' carbon disulfide capacity dropped sharply during 1991 when Akzo Chemicals closed down a 159,000 ton per year plant at Delaware City, Delaware (126). The United States' carbon disulfide industry still accounts for about 12% of the total worldwide installed capacity.

Table 2. Estimated Installed Carbon Disulfide Capacity, 1991^a

	Hydrocarbon–sulfur process		Charcoal–sulfur process	
	Number of plants	Capacity, 10 ³	Number of plants	Capacity, 10 ³
		t y		t y
North and Central America	5	185	2	5
South America	1	14	9	40
Europe and Africa	10	767	8	55
Asia	2	86 ^b	16	135
<i>Total</i>	<i>18</i>	<i>1052</i>	<i>35</i>	<i>235</i>

^a Refs. 123, 124.

^b Includes a 26,000-t plant scheduled for 1992 completion.

Table 3. Principal Manufacturers of Carbon Disulfide by the Hydrocarbon–Sulfur Process, 1991

Producer	Location	Estimated annual capacity, 10 ³
t		
<i>North America</i>		
Akzo Chemicals	LeMoyne, Ala.	113
PPG Industries	Natrium, W. Va.	27
Atochem North America	Green Bayou, Tex.	18
Cornwall Chem. (Akzo)	Comwall, Ontario	23
Thio-Pet Chemicals	Fort Saskatchewan, Alberta	4

<i>Total</i>		185
<i>Europe</i>		
Courtaulds	Manchester, UK	85
Carbosulf Chemische	Cologne, Germany	82
Rhone-Poulenc	Roches-de-Condrieu, France	120
Rhone-Poulenc	Kallo (Antwerp), Belgium	60
Foret SA (FMC)	Barcelona, Spain	40
State Authority	Grzybow, Poland	200
State Authority	Braila, Romania	40
State Authority	Vrasa, Bulgaria	20
State Authority	Sokol, Russia	60
State Authority	Volgograd, Russia	60
<i>Total</i>		767
<i>Other countries</i>		
I.Q. Duperial SAIC	San Lorenzo, Argentina	14
Nippon Ryutan Kogyo KK	Tsurusaki, Oita, Japan	60
State Authority	Liaoyang, Liaoning, China	26 ^a
<i>Total</i>		100
<i>World total</i>		1052

^a Completion scheduled 1992 (125).

The production and price history for carbon disulfide in the United States appears in Table 4. Production peaked at 362,000 t yr in 1969 and had fallen to less than half that amount by 1991. The cost for producing carbon disulfide is sensitive to sulfur and natural gas prices, which have increased greatly since about 1974. The future demand for carbon disulfide is strongly tied to the fate of its principal use, the production of regenerated cellulose products.

Table 4. U.S. Production and Prices of Carbon Disulfide^a

Year	Amount, 10 ³ t	Bulk price, \$ t
1940	91	99
1950	193	97
1960	237	120
1970	327	107
1980	171	259
1988	161	463
1990	136	463
1991		491

^a Refs. 127–129.

Production of carbon disulfide expanded rapidly after World War II to supply the growing needs of the viscose rayon industry, which consumes about 0.31 ton CS₂ per ton rayon. The high plant capacities obtainable with the methane–sulfur route resulted in consolidation of the carbon disulfide industries in the United States and Western Europe, where a few producers now account for the bulk of the capacity (see Table 3). Some rayon manufacturers produce their own carbon disulfide. Rayon enjoys an extensive international market that can affect local CS₂ manufacturers. Competition from noncellulosic synthetic fibers has caused a drop in rayon production in the United States since the mid-1960s. One rayon plant in the United States closed in 1989 as a result of environmental concerns. However, plans have been announced to build a new rayon plant in Louisiana (130) that is expected to achieve improved carbon disulfide utilization and low emissions by recovering and recycling carbon disulfide. This pattern of modern viscose rayon plants replacing aging facilities that cannot be economically upgraded is apt to be repeated in other parts of the world. In a development that could have far-ranging implications, a viscose rayon producer is constructing a solvent spun cellulosic fiber plant using an amine oxide solvent rather than carbon disulfide (131,132).

Use of carbon disulfide for manufacture of cellophane [9005-81-6] has dropped dramatically because of competition from plastic films, and just one cellophane producer, Flexel, Inc., remains in the United States.

Carbon disulfide for manufacture of carbon tetrachloride increased in the 1950s and 1960s to supply the key raw material for chlorofluorocarbon refrigerants and aerosol propellants. Because of ecological and health concerns, carbon tetrachloride consumption began to decline in the mid-1970s. That use for carbon disulfide will suffer under a United Nations proposal to phase out carbon tetrachloride and chlorofluorocarbons to protect the earth's ozone layer (133). During 1991 the only remaining carbon tetrachloride plant in the United States that employed the carbon disulfide route was permanently shut down. Consumption of carbon disulfide in rubber, agriculture, mining, and specialty industrial applications is anticipated to remain close to 1991 levels for the next several years.

Specifications and Quality Control

Modern plants generally produce carbon disulfide of about 99.99% purity. High product quality is ensured by closely controlled continuous fractional distillation. Reagent and U.S. Federal specifications, and typical commercial-grade quality are listed in Table 5.

Table 5. Carbon Disulfide Specifications

Property	Method	Technical industry, typical	Technical, U.S. Federal ^a	Reagent, ACS ^b
specific gravity	pycnometer	1.270–1.272 ^c	1.262–1.267 ^d	
residue	dry at 60°C	0.002% max	10 mg 100 mL	0.002% max
color	APHA, Pt–Co 500 std	<20 ^e	special test	10 max
boiling range, °C	ACS distillation	45.5–47.5	45.5–47.5	1°C incl. 46.3 ± 0.1°C
foreign sulfide	lead acetate test	negative		
foreign sulfide	special tests		no discoloration of copper	

H ₂ S and SO ₂	iodine color test		passes
water, %	Karl Fischer	no turbidity	0.05% max
^a Ref. 134.			
^b Ref. 135. USP specifies ACS reagent-grade.			
^c 15 °C.			
^d 20 °C.			
^e Light transmission vs water 98% minimum is sometimes used as a specification.			

Toxicology, Health, and Safety Factors

Care must be exercised in handling carbon disulfide because of both health concerns and the danger of fire or explosions. Occupational exposure potentially may involve as many as 20,000 workers in the United States (136). Ingestion is rare, but a 10 mL dose can prove fatal (137). Contact usually occurs by inhalation of vapor. However, vapor and liquid can be absorbed through intact skin and poisoning may occur by the dermal route (138). Repeated contact of liquid carbon disulfide with the skin can cause inflammation and cracking because carbon disulfide removes protective waxes and oils. Extended skin contact results in blistering and possibly second- and third-degree burns. Precautions should be taken to avoid breathing of vapors or mists that may contain carbon disulfide. Contact with skin or eyes should also be avoided, and adequate safety gear should be worn, including goggles, impervious gloves, and appropriate clothing. Contact lenses should be removed before going into any area where exposure to carbon disulfide might occur. A chemical cartridge respirator with an organic vapor cartridge can offer protection up to 50 ppm carbon disulfide in air. Above that level or in entering areas of unknown vapor concentrations, a self-contained breathing apparatus should be worn, with careful attention given to possible explosion hazards (139).

The odor threshold of carbon disulfide is about 1 ppm in air but varies widely depending on individual sensitivity and purity of the carbon disulfide. However, using the sense of smell to detect excessive concentrations of carbon disulfide is unreliable because of the frequent co-presence of hydrogen sulfide that dulls the olfactory sense.

Immediate effects of overexposure to carbon disulfide vapors range from headache, dizziness, nausea, and vomiting to life-threatening convulsions, unconsciousness, and respiratory paralysis. For an exposure time of 30 min, 1150 ppm carbon disulfide in air results in serious symptoms, 3210 ppm is dangerous to life, and 4815 ppm is fatal (140). Prolonged and repeated exposure to carbon disulfide vapor can affect both the central and peripheral nervous systems. Manifestations of long-term overexposure may include headache, vertigo, irritability, nervousness, depression, mental derangement, memory loss, muscular weakness, fatigue, insomnia, eating disorders, gastrointestinal disturbances, impaired vision, diminished reflexes, numbness, and difficulty walking. Certain workers exposed to a time-weighted average of 11 ppm experienced headaches and dizziness, and those with an average of 186 ppm had additional complaints of nervousness, fatigue, sleep problems, and weight loss (141). Repeated exposure to relatively high concentrations of carbon disulfide has long been known to cause serious neurological and psychological impairments. In recent years, previously unrecognized and more subtle toxic effects of repeated lower level exposures became evident. This led OSHA in 1989 to reduce permissible concentration limits to 4 ppm (12 mg m⁻³) maximum time-weighted average for 8-h exposure and 12 ppm (36 mg m⁻³) maximum for 15 min short-term exposure (138). Compliance with both limits is preferably achieved by engineering and work practice controls, although respirators are acceptable in certain specific operations. OSHA states the new limits should substantially reduce the risk of both cardiovascular disease and adverse reproductive effects associated with carbon disulfide. Analysis of urine specimens for carbon disulfide metabolites by an iodine–azide test (142) and other methods (143) can indicate overexposure.

Health hazards linked to carbon disulfide are extensively covered (136). Also available are epidemiological studies (144–146), general reviews containing many references (147–150), and a Material Safety Data Sheet (151).

Uses

United States consumption of carbon disulfide totaled about 108,000 t in 1990 according to SRI International, with the following distribution by end use application: 46,000 tons for rayon; 33,000 tons for carbon tetrachloride; 12,000 tons for rubber; 5,000 tons for cellophane; and 12,000 tons for agricultural and miscellaneous uses (129). During 1991 the carbon tetrachloride application disappeared entirely thereby reducing the annualized carbon disulfide usage to an estimated 75,000 tons. Net exports are around 6,000 tons, and are expected to increase in the future.

Carbon disulfide is used to make intermediates in the manufacture of rubber vulcanization accelerators, including MTB (2-mercaptobenzothiazole [149-30-4]), thiocarbanilide, and dimethyl dithiocarbamate salts (see RUBBER CHEMICALS). Thiocarbanilide is also used in dyes. Thiophosgene (thiocarbonyl chloride), made from carbon disulfide, is a useful intermediate in the synthesis of many organic sulfur compounds. Xanthates (dithiocarbonates) produced from carbon disulfide are widely employed as flotation chemicals for metal sulfide ores in the mining industry. The solvent properties of carbon disulfide find a wide range of industrial uses, including various dehydration, extraction, reaction, and separation applications. A useful laboratory chemical, carbon disulfide is a reactant in the synthesis of many compounds and a solvent in Friedel-Crafts reactions. Its solvent properties are useful in spectroscopy and in solubilizing phosphorus and sulfur.

Pharmaceutical intermediates, such as thiocarbanilide and thiocyanates, are prepared from carbon disulfide. Methionine [59-51-8], an essential amino acid, is manufactured from carbon disulfide intermediates. At one time carbon disulfide was commonly used in combination with chlorinated hydrocarbons as a grain fumigant, but that application was suspended in 1985 by the United States Environmental Protection Agency. Carbon disulfide is a starting material for several fungicides, soil fumigants, and insecticides or their intermediates, such as trichloromethanesulfenyl chloride, disodium ethylenebis(dithiocarbamate), sodium methylthiocarbamate, ammonium dithiocarbamate, and thiocyanate salts. The thiocyanates also have many nonagricultural uses.

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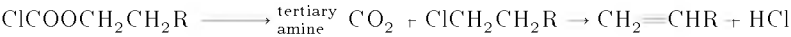
Chloroformate	Mol wt	Sp gr, d_{4}^{20}	Refractive index n_D^{20}	Flash point, °C		Viscosity, mPa·s (=cP), 20°C	Bp, °C at		
				TOC a	TCC b		2.67 kPa ^c	13.3 kPa ^c	101. 3 kPa ^c
methyl chloroformate	94.5	1.250	1.3864	24.4	17.8				71
ethyl chloroformate	108.5	1.138	1.3950	27.8	18.3				94
isopropyl chloroformate	122.5	1.078	1.3974	27.8	23.3	0.65		47	105
<i>n</i> -propyl chloroformate	122.5	1.091	1.4045	34.4		0.80	25.3	57.5	112.
allyl chloroformate	120.5	1.139	1.4223	27.8	31.1	0.71	25	57	4
<i>n</i> -butyl chloroformate	136.5	1.058	1.4106	52.2	46.0	0.888	44	77.6	
<i>sec</i> -butyl chloroformate	136.5	1.049	1.4560	35.6	38.0	0.897	36	69	
isobutyl chloroformate	136.5	1.047	1.4079	39.5	34.4	0.88	39	71	
2-ethylhexyl chloroformate	192.7	0.991	1.4307		86.0	1.774	98	137	
<i>n</i> -decyl chloroformate	220.7	0.973	1.4400	118.3	120.2	3.00	122	159	
phenyl chloroformate	156.5	1.247	1.5115		77.0	1.882	83.5	121	185
benzyl chloroformate	170.6	1.216	1.5175	80.0	107.9	2.57	103	123	152
ethylene bis chloroformate	186.9	1.470	1.4512	134.0	126.0	4.78	108	137	
diethylene glycol bis chloroformate	231.0	1.388	1.4550	160.0	182.2	8.76	148	180	

^a Tag open cup.
^b Tag closed cup.
^c To convert kPa to mm Hg, multiply by 7.50.

Chemical Properties

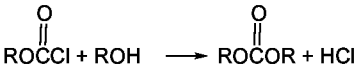
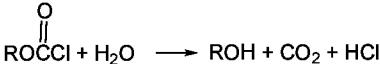
Chloroformates are reactive intermediates that combine acid chloride and ester functions. They undergo many reactions similar to those of acid chlorides; however, the rates are usually slower (4–8). Those containing smaller organic (hydrocarbon) substituents react faster than those containing large organic (hydrocarbon) substituents (3). Reactions of chloroformates and other acid chlorides proceed faster with better yields when alkali hydroxides or tertiary amines are present to react with the HCl as it forms. These bases act as stoichiometric acid acceptors rather than as true catalysts.

Stability. The ester moiety determines thermal stability generally in the following order of decreasing stability: aryl > primary alkyl > secondary alkyl > tertiary alkyl. In terms of mechanistic chemistry the chloroformates that produce stable carbonium ions on thermal decomposition, eg, benzyl, isopropyl, or tertiary butyl, are unstable (9). Thus iron, zinc, and aluminum chlorides, ie, Lewis acids, catalyze decomposition of chloroformates and therefore the chloroformates should be handled in the absence of metals. Alkyl chloroformates can be purified easily by distilling in glass vessels, but secondary or benzylic chloroformates have to be distilled under high vacuum in glass vessels. Tertiary chloroformates are too unstable to distill, even under high vacuum. Decomposition of chloroformates may also be initiated by tertiary amines such as pyridine or quinoline (10).

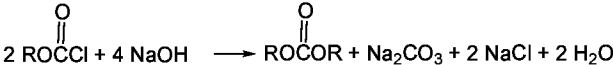


Reactions with Oxygen Moieties.

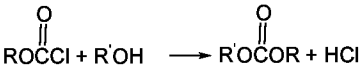
Hydroxylic Compounds. Chloroformates on reaction with water give the parent hydroxy compound, HCl, and CO₂ as well as the symmetrical carbonate formed by the reaction of the hydroxy compound with chloroformate.

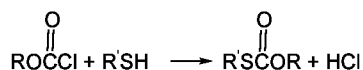


Alkali Metal Hydroxides. Addition of base to aqueous chloroformates catalyzes hydrolysis to yield the parent hydroxy compound (11). However, the use of a stoichiometric amount of alkali metal hydroxides can lead to the symmetrical carbonate, especially from aryl chloroformates (12,13).



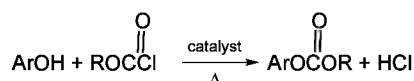
Aliphatic Alcohols and Thiols. Aliphatic alcohols on reaction with chloroformates give carbonates and hydrogen chloride. Frequently, the reaction proceeds at room temperature without a catalyst or hydrogen chloride acceptor. However, faster reactions and better yields are obtained in the presence of alkali metals or their hydroxides, or tertiary amines. Reactions of chloroformates with thiols yield monothiolocarbonates (14).



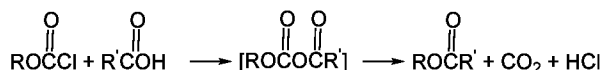


Heterocyclic Alcohols. Their reactions with chloroformates lead to carbonates. Thus furan- and tetrahydrofuran-derived alcohols give the corresponding carbonates in 75% yield (15). Inorganic bases and tertiary amines as acid acceptors increase the rate and yield in this reaction.

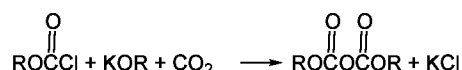
Phenols. Phenols are unreactive toward chloroformates at room temperature and at elevated temperatures the yields of carbonates are relatively poor (<10%) in the absence of catalysis. Many catalysts have been claimed in the patent literature that lead to high yields of carbonates from phenol and chloroformates. The use of catalyst is even more essential in the reaction of phenols and aryl chloroformates. Among the catalysts claimed are amphoteric metals or their halides (16), magnesium halides (17), magnesium or manganese (18), secondary or tertiary amines such as imidazole (19), pyridine, quinoline, picoline (20–22), heterocyclic basic compounds (23) and carbonamides, thiocarbonamides, phosphoramides, and sulfonamides (24).



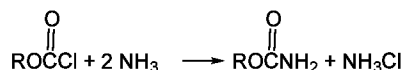
Carboxylic Acids. Esters are the main products in the reaction of chloroformates with carboxylic acids. The intermediate mixed carboxylic–carbonic anhydrides are very active acylating agents (25–27) but these agents may be isolated in cold temperatures for producing useful products (28).



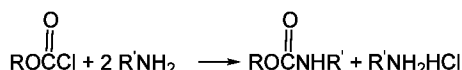
Pyrocarbonates or dicarbonates (anhydrides of carbonic acids) have been prepared as follows (29):



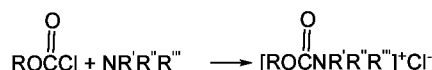
Reactions with Nitrogen Compounds. The reaction with ammonia is the classical method for preparing primary carbamates. Excess ammonia is used as an acid acceptor to remove the HCl formed (see CARBAMIC ACID).



Amines. Primary and secondary aliphatic amines also yield carbamates in the presence of excess amine or other acid acceptors such as inorganic bases. Aromatic primary and secondary amines and heterocyclic amines react similarly, although slowly.

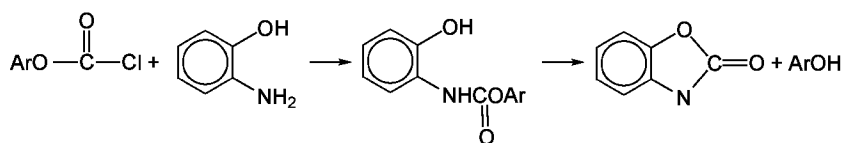


Tertiary amines give quaternary ammonium compounds.



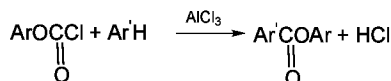
Amino Alcohols. Reaction of chloroformate is much more rapid at the amino group than at the hydroxyl group (4–8). Thus the hydroxy carbamates, which can be cyclized with base to yield 2-oxazolidones, can be selectively prepared (29). Nonionic detergents may be prepared from poly[(ethylene glycol) bis(chloroformates)] and long-chain tertiary amino alcohols (30).

Aminophenols. Reaction of chloroformate with aminophenols (qv) also takes place at the more reactive amino group selectively. Thus *o*-aminophenol [95-55-6] gives benzoxazolone [59-49-4] by cyclization of the intermediate carbamate (31).

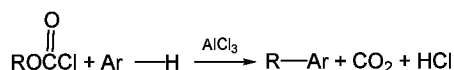


Amino Acids. Chloroformates play a most important role for the protection of the amino group of amino acids (qv) during peptide synthesis (32). The protective carbamate formed by the reaction of benzyl chloroformate and amino acid (33) can be cleaved by hydrogenolysis to free the amine after the carboxyl group has reacted further. The selectivity of the amino groups toward chloroformates results in amino-protected amino acids with the other reactive groups unprotected (34,35). Methods for the preparation of protected amino acids on an industrial scale have been developed (36,37). A wide variety of chloroformates have been used that give various carbamates that are stable or cleaved under different conditions.

Acylation. Aryl chloroformates are good acylating agents, reacting with aromatic hydrocarbons under Friedel-Crafts conditions to give the expected aryl esters of the aromatic acid (38).

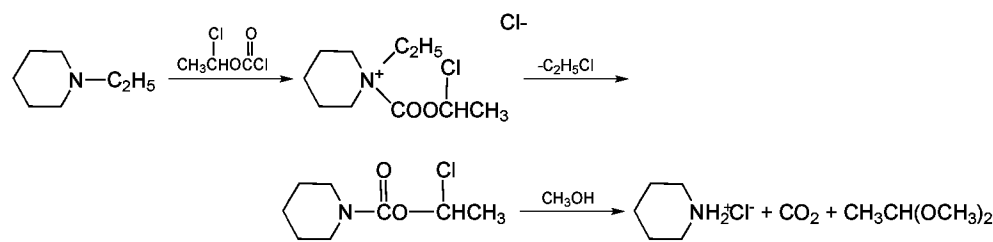


However, with aliphatic chloroformates under similar conditions, alkylation takes place (39).

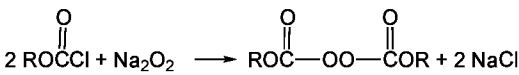


Dealkylation. Chloroformates such as vinyl chloroformates (40) are used to dealkylate tertiary amines. Chloroformates are superior to the typical Von Braun reagent, cyanogen bromide, because of increased selectivity producing cleaner products. Other chloroformates such as allyl, methyl, phenyl, and trichloroethyl have also been used in dealkylation reactions. Although the dealkylation reaction using chloroformates is mostly carried out on tertiary amines, dealkylation of oxygen or sulfur centers, ie, ethers or thioethers, can also be achieved. α -Chloroethyl chloroformate [50893-53-3] (ACE-Cl) (41,42) is superior to all previously used chloroformates for the dealkylation reaction. ACE-Cl has the advantage that the conditions required for ACE

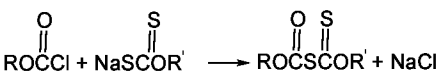
removal are much milder, thus expanding the list of functionalities allowed in the amine to be dealkylated (43). The potential significance of this process in drug congener preparation has been outlined (44).



Miscellaneous Reactions. Epoxy compounds yield chlorosubstituted carbonates (45). The reaction of chloroformates with hydrogen peroxide or metal peroxides results in the formation of peroxydicarbonates that are used as free-radical initiators of polymerization of vinyl chloride, ethylene, and other unsaturated monomers (46,47).



The reaction of chloroformates with sodium xanthates results in the formation of alkyl xanthogen formates that are useful as flotation agents in extraction of metals from their ores (48).



Manufacture

The reaction of phosgene with alcohols or phenols has been thoroughly discussed (1). Alkyl chloroformates, especially those of low molecular weight alcohols, are prepared by the reaction of liquid anhydrous alcohols with molar excess of dry, chlorine-free phosgene at low temperature. Corrosion-resistant reactors, lines, pumps, and valves are required. Materials of construction include glass, porcelain, Hastelloy C, Teflon-lined steel, or chemically impregnated carbon on steel such as Karbate. Temperatures are kept at 0–10°C for the lower alcohols and may rise to 60°C for the higher aliphatic alcohols. Hydrogen chloride is evolved as the reaction proceeds and is then absorbed in a tower after recovering excess phosgene. The reactions are most often run in batch reactors, although some of the high volume chloroformates are produced in cascade-type continuous reactors (49,50). The continuous reactors also ensure excess of phosgene at all times since both reactants are added simultaneously, thus minimizing dialkylcarbonate side products. Phenols react with phosgene with difficulty and usually require higher temperature and lead to a fair amount of diaryl carbonate as a side product. Many different catalysts have been used to reduce the reaction temperature and the carbonate side products (51–53). Chloroalkyl chloroformates have been synthesized by the reaction of aldehydes with phosgene (41,42,54).

Unreacted phosgene is removed from the crude chloroformates by vacuum stripping or gas purging. Chloroformates of lower primary alcohols are distillable; however, heavy-metal contamination should be avoided. As stated earlier, chloroformates generating a stable carbonium ion on decomposition, ie, secondary or tertiary chloroformates or benzylic chloroformates, are especially unstable in the presence of heavy metals and more specifically Lewis acids and, hence, should be distilled at as low a temperature and high vacuum as possible.

The yields of primary chloroformates are usually well above 90% . The secondary chloroformates give yields of 80–90% . In cases where the alcohols are most unreactive, an acid acceptor may be used to drive the reaction. Commercial processes are usually run neat, although solvents such as chloroform, toluene, dioxane, or THF are sometimes used to dissolve the starting alcohol or the product chloroformate as may be necessary.

Shipping and Storage

Chloroformates are shipped in nonreturnable 208-L (55-gal) polyethylene drums with carbon steel overpacks or high density polyethylene drums. For bulk shipments, insulated stainless-steel tank containers and trucks provide secure protection. Tank truck and rail car quantities are shipped using equipment dedicated for these types of products. Materials such as isopropyl chloroformate, benzyl chloroformate, and *sec*-butyl chloroformate that require refrigeration are precooled when shipped in bulk containers. Bulk shipments that are precooled must proceed to the destination without layover. Drum shipments of IPCF, BCF, and SBCF must be shipped in refrigerated containers. Many of the chloroformates are only shipped in truck load shipments. The U.S. Department of Transportation (DOT) Hazardous Materials Regulations control the shipments of chloroformates, as described in Table 3.

Table 3. Department of Transportation Regulations for Chloroformate Shipment

Type	DOT hazard class	Subsidiary risk 1	Subsidiary risk 2	Tank truck	Refrigeration
allyl chloroformate	corrosive	poison	flammable	no	needed to pre-serve assay
benzyl chloroformate	corrosive material			no	needed
diethylene glycol				yes	needed to pre-serve
bischloroformate					assay ^a
ethyl chloroformate	poison	flammable	corrosive	b	
2-ethylhexyl chloroformate	poison	corrosive		yes	
hexanediol bischloroformate				yes	
isobutyl chloroformate	poison	flammable	corrosive	b	
isopropyl chloroformate	corrosive	poison	flammable	b	needed
methyl chloroformate	poison liquid	flammable	corrosive	b	
<i>n</i> -propyl chloroformate	poison	flammable	corrosive	b	
phenyl chloroformate				yes	
<i>sec</i> -butyl chloroformate	poison	flammable	corrosive	b	needed

^a Only for shipments through the tropics.
^b Bulk shipments can be made in DOT-approved IMO containers.

Chloroformates should be stored in a cool, dry atmosphere, preferably refrigerated, especially for prolonged storage. They should be transferred

from containers to storage tanks or reactors through a closed system, using stainless steel, nickel, glass or Hastelloy pumps, lines, and valves.

Economic Aspects

Most chloroformate production is used captively and production figures are not available. The prices are also not published, but can be obtained by contacting U.S. and other worldwide producers, such as PPG Industries, Inc., BASF, Van Cham, and SNPE.

Specifications and Analysis

Table 4 lists the specifications of commercial chloroformates. The lower boiling chloroformates are analyzed by gas–liquid chromatography. Higher molecular weight chloroformates are first hydrolyzed and then analyzed by titration, using the Volhard method.

Table 4. Typical Specifications of Commercial Chloroformates

Assay	Value
purity, ° o	98
phosgene, ° o	<0.1
iron, ppm	<10
acidity as HCl, ° o	<0.1
alcohol or phenol, ° o	<2

Toxicity

Chloroformates, especially those of low molecular weight, are lachrimators, vesicants, and produce effects similar to those of hydrogen chloride or carboxylic acid chlorides. They can also irritate the skin and mucous membranes, producing severe burns and possible irreversible tissue damage. Inhalation of vapors of lower chloroformates result in coughing, choking, and respiratory distress, and, with some chloroformates like methyl chloroformate, inhalation can be fatal as a result of the onset of pulmonary edema, which may not appear for several hours after exposure (55). Table 5 gives the acute toxicities of some chloroformates (55–57).

Table 5. LD₅₀ of Some Chloroformates

Chloroformate	Oral, mg kg	Dermal, mg kg	Inhalation, mg L ^a
methyl	40	>3038	0.45
ethyl	411	>2000	1.09
<i>n</i> -propyl	650	>10200	1.6
isopropyl	177.8	11300	1.5
<i>sec</i> -butyl	1030	2025	1.82
isobutyl	2500	>2500	1.8
2-ethylhexyl	3038	>3038	>3.44
allyl	178	1470	<2
phenyl	1581	>3300	>1.5
benzyl	5000	2065	>2.1
ethylene bis	1100	2000	
diethylene glycol bis	813.2	3400	

^a For 1-h exposure (mg L of air).

Uses

Chloroformates are versatile, synthetic intermediates, based on the affinity of the chlorine atoms for active hydrogen atoms. Chloroformates should be considered as intermediates for syntheses of pesticides, perfumes, drugs, polymers, dyes, and other chemicals. Some of these products, eg, carbonates, are used as solvents, plasticizers, or as intermediates for further synthesis. A significant use of chloroformates is for conversion to peroxydicarbonates, which serve as free-radical initiators for the polymerization of vinyl chloride, ethylene, and other unsaturated monomers. The most widely used percarbonate initiators are diisopropyl peroxydicarbonate (IPP), di-2-ethylhexyl peroxydicarbonate (2-EHP), and di-*sec*-butyl peroxydicarbonate (SBP). The following list includes most of the commercially used percarbonates.

Percarbonate	CAS Registry Number
diethyl percarbonate	[14666-78-5]
diisopropyl (IPP) percarbonate	[105-64-6]
di- <i>n</i> -butyl percarbonate	[1621549-9]
di- <i>sec</i> -butyl (SBP) percarbonate	[19910465-7]
dicyclohexyl percarbonate	[156149-5]
di-4- <i>t</i> -butylcyclohexyl percarbonate	[2652373-9]
di- <i>n</i> -hexadecyl percarbonate	[2632214-5]
di- <i>n</i> -propyl (NPP) percarbonate	[1606638-9]
di-2-ethylhexyl (2-EHP) percarbonate	[1611162-9]

Carbamates derived from chloroformates are used to manufacture pharmaceuticals, including tranquilizers (58), antihypotensives, and local anesthetics, pesticides, and insecticides (see CARBAMIC ACID). Ethyl chloroformate is used in the manufacture of ore flotation agents by reaction with various xanthates (48). Diethylene glycol bis(chloroformate) [106-75-2] is the starting material for diethylene glycol bis(allyl carbonate) [142-22-3], CR-39, or Nouryset 200, monomer, used in the manufacture of break-resistant optical lenses, which is obtained by the reaction with allyl alcohol [107-18-6] (59). Alternatively, it can be obtained from allyl chloroformate [2937-50-0] and diethylene glycol (60) (see ALLYL MONOMERS AND POLYMERS). Bis(chloroformic esters) condense with diamines to give polyurethanes (60) (see URETHANE POLYMERS). Blowing agents for producing foam rubber, polyethylene, and vinyl chloride are made from chloroformates, hydrazine, and a base. For example,

diisopropyl azidoformate [2446-83-5] is made from isopropyl chloroformate (61). The use of chloroformates as blocking agents for amino acids (33–37) has become significant in the synthesis of peptides for medicinal purposes, as well as in the synthesis of artificial sweeteners such as aspartame.

CARBONATES

Chloroformates and alcohols or phenols give carbonic diesters. In addition, the higher diesters can be made from the lower ones by alcoholysis or ester interchange by heating the lower diester with a higher alcohol in the presence of acid such as HCl or H₂SO₄, or base such as sodium alcoholate. The driving force for these reactions is the formation of lower alcohols that can be distilled off. Mixed diesters can be prepared by treating a chloroformate with an alcohol or phenol having a different radical.

More recently, preparation of carbonic esters by nonphosgene routes, such as the reactions of CO or CO₂ with appropriate substances in the presence of catalysts, has been preferred. These methods are more economic in many cases and naturally less hazardous than phosgene routes.

Carbonates are indexed in *Chemical Abstracts* under carbonic acid, esters. Symmetrical diesters have the prefix di or bis. Unsymmetrical diesters are listed with the two radicals following each other. For example, ethyl phenyl carbonic diester is C₂H₅OCOOC H₅. Table 6 lists commonly used carbonates, their *Chemical Abstracts* Service Registry Number, and formulas.

Table 6. Carbonates

Carbonate	CAS registry number	Formula
dimethyl carbonate	[616-38-6]	CH ₃ OCOOCH ₃
diethyl carbonate	[105-58-8]	C ₂ H ₅ OCOOC ₂ H ₅
divinyl carbonate	[7570-02-7]	CH ₂ =CHOCOCH=CH ₂
di- <i>n</i> -propyl carbonate	[623-96-1]	CH ₃ CH ₂ CH ₂ OCOOCH ₂ CH ₂ CH ₃
diisopropyl carbonate	[6482-34-4]	(CH ₃) ₂ CHOCOCH(CH ₃) ₂
diallyl carbonate	[15022-08-9]	CH ₂ =CHCH ₂ OCOOCH ₂ CH=CH ₂
methyl allyl carbonate	[35466-83-2]	CH ₃ OCOCH ₂ CH=CH ₂
diisobutyl carbonate	[539-92-4]	(CH ₃) ₂ CHCH ₂ OCOOCH ₂ CH(CH ₃) ₂
isobutyl propyl carbonate	[40882-93-7]	CH ₃ CH(CH ₃)CH ₂ OCOOCH ₂ CH ₂ CH ₃
di- <i>tert</i> -butyl carbonate	[34619-03-9]	(CH ₃) ₃ COCOOC(CH ₃) ₃
di- <i>sec</i> -butyl carbonate	[623-63-2]	CH ₃ CH ₂ CH(CH ₃)OCOCH(CH ₃)CH ₂ CH ₃
di- <i>n</i> -butyl carbonate	[542-52-9]	CH ₃ CH ₂ CH ₂ CH ₂ OCOOCH ₂ CH ₂ CH ₂ CH ₃
hexyl methyl carbonate	[39511-75-6]	CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ OCOOCH ₃
pentyl propyl carbonate	[40882-94-8]	CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ OCOOCH ₂ CH ₂ CH ₃
didodecyl carbonate	[6627-45-8]	CH ₃ (CH ₂) ₁₀ CH ₂ OCOOCH ₂ (CH ₂) ₁₀ CH ₃
diphenyl carbonate	[102-09-0]	C ₆ H ₅ OCOOC C ₆ H ₅
phenyl allyl carbonate	[16308-68-2]	C ₆ H ₅ OCOCH ₂ CH=CH ₂
vinyl ethyl carbonate	[7670-06-1]	CH ₂ =CHOCOOC ₂ H ₅
ethyl phenyl carbonate	[3878-46-4]	C ₂ H ₅ OCOOC C ₆ H ₅
ethylene carbonate	[96-49-1]	OCOOCH₂CH₂
allyl diglycol ^a carbonate	[142-22-3]	O(CH ₂ CH ₂ OCOOCH ₂ CH=CH ₂) ₂
ditolyl ^b carbonate	[41903-18-8]	CH ₃ C ₆ H ₄ OCOOC C ₆ H ₄ CH ₃
dibenzyl carbonate	[3459-92-5]	C ₆ H ₅ CH ₂ OCOOCH ₂ C ₆ H ₅
di-2-ethylhexyl carbonate	[14858-73-2]	CH ₃ (CH ₂) ₃ CH(C ₂ H ₅)CH ₂ OCOOCH ₂ CH(C ₂ H ₅)(CH ₂) ₃ CH ₃

^a Diethylene glycol bis(allylcarbonate).
^b Diethylene glycol bis(tolylcarbonate).

Properties

The physical properties of selected carbonates are given in Table 7. The lower alkyl carbonates are neutral, colorless liquids with a mild sweet odor. Aryl carbonates are normally solids.

Table 7. Physical Properties of Selected Carbonates

Carbonates	Mol wt	Sp gr, <i>d</i> ₄ ²⁰	Refractive index <i>n</i> _D ^c	Flash point °C	Viscosity ^a mPa·s(–cP)	Bp, °C ^b
dimethyl	90.08	1.073	1.3697 ^c	21.7 ^d 16.7 ^e	0.664 (20)	90.2
diethyl	118.13	0.975	1.3846 ^c	46.1 ^d 32.8 ^e	0.868 (15)	23.8 (1.33) 69.7 (13.33) 126.8
di- <i>n</i> -propyl	146.18	0.941	1.4022 ^c	64 ^e	^f	165.5–166.6
diisopropyl	146.18					147.0
diallyl	142.15	0.994	1.4280 ^c			97 (8.13) 105 (13.33) 166 (97.31)
di- <i>n</i> -butyl	174.14	0.9244	1.4099 ^g			207.7
di-2-ethylhexyl	204.19	0.8974 ²⁰ ₂₀	1.4352 ^g			173 (1.33) 302
diphenyl	214.08	0.8974 ⁸⁷ ₄				160 (0.27)
diethylene glycol bis(allyl)	274.3	1.143	1.4503	177 ^h	9 (25)	

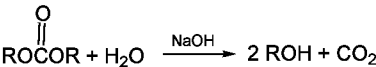
tolyl diglycol	374.4	1.189	1.5229 ^g	247–248
ethylene	88.06	1.3218 ³⁹ ₄	1.4158 ⁱ	(0.27) 248

^a At the temperature noted in parentheses (°C).
^b At 101.3 kPa (– 1 atm) unless otherwise noted in parentheses in kPa.
^c Ref. 16.
^d Tap open cup.
^e Tag closed up.
^f Brookfield no. 1 spindle; rpm (mPa·s) 10(5), 20(6.5), 50(8.0), 100(12.0).
^g Ref. 21.
^h Cleveland open cup.
ⁱ Ref. 25.

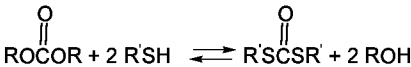
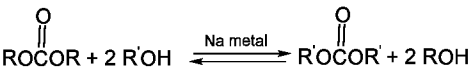
Chemical Properties

Carbonates undergo nucleophilic substitution reactions analogous to chloroformates except in this case, an OR group (rather than chloride) is replaced by a more basic group. Normally these reactions are catalyzed by bases. Carbonates are sometimes preferred over chloroformates because formation of hydrogen chloride as a by-product is avoided, which simplifies handling. However, the reactivity of carbonates toward nucleophiles is considerably less than chloroformates.

Reaction with Water. The alkyl carbonate esters, especially the lower ones, hydrolyze very slowly in water when compared to the carbonochloridic esters (chloroformates). Under alkaline conditions, the rates of hydrolysis are similar to those of the corresponding acetic acid esters.

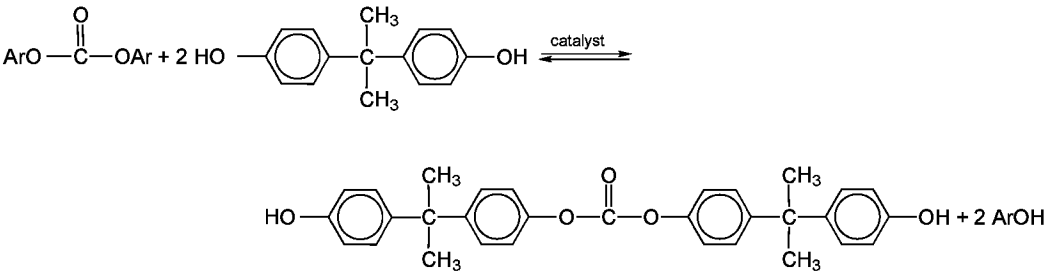


Reaction with Alcohols and Thiols. Lower molecular weight carbonates react with alcohols and thiols to produce higher molecular weight carbonates. These reactions are catalyzed by the usual transesterification catalysts such as sodium metal. Also, as a practical matter, these reactions are driven to completion by removing lower boiling alcohol and thus can be used to convert lower molecular weight carbonates to the higher molecular weight ones.

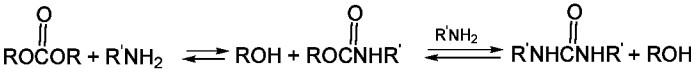


Transesterification has become a convenient method for synthesizing high alkyl, aryl, or alkyl aryl carbonates. Fiber- and film-forming polycarbonates are produced by transesterifying dialkyl, dicycloalkyl, or diaryl carbonates with alkyl, cycloalkyl, or aryl dihydroxy compounds (62).

Reaction with Phenols. Phenols react with diphenyl carbonate in the presence of bases or organometallic catalysts to produce diaryl carbonates. A specific example is the reaction of diphenyl carbonate with bisphenol A [80-05-7] to produce polycarbonate.

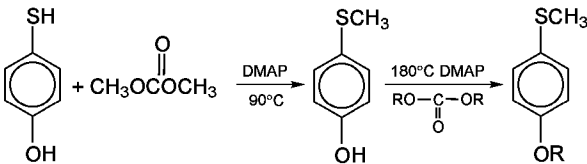


Reaction with Amines and Ammonia. Carbonates react with amines and ammonia to produce carbamates or ureas. This reaction can be used as an alternative route to producing carbamate pesticides.



Alkylation. Dialkyl carbonates react with a variety of functional groups to produce the alkylated derivatives (63). The reaction of dimethyl carbonate as a methylating agent has received much attention (63–75). This method offers the advantage of the typical methylating agents, such as dimethyl sulfate or methyl iodide, that are much more hazardous. Methylation reactions with dimethyl carbonate require high temperatures (120–220°) and further require use of catalyst 4-dimethylaminopyridine [1122-58-3] (DMAP). Only the sulfur and selenium compounds do not require high temperatures for methylation.

As seen in Figure 1, the organo sulfur compounds are methylated at the boiling point (90°C) of dimethyl carbonate, whereas methylation (or alkylation with other alkyl groups) of other functional groups requires higher temperatures. This has resulted in the selective methylation of sulphydryl groups of compounds that contain other substituents that can be alkylated. The other substituents can then be alkylated at elevated temperatures (63). Thus,



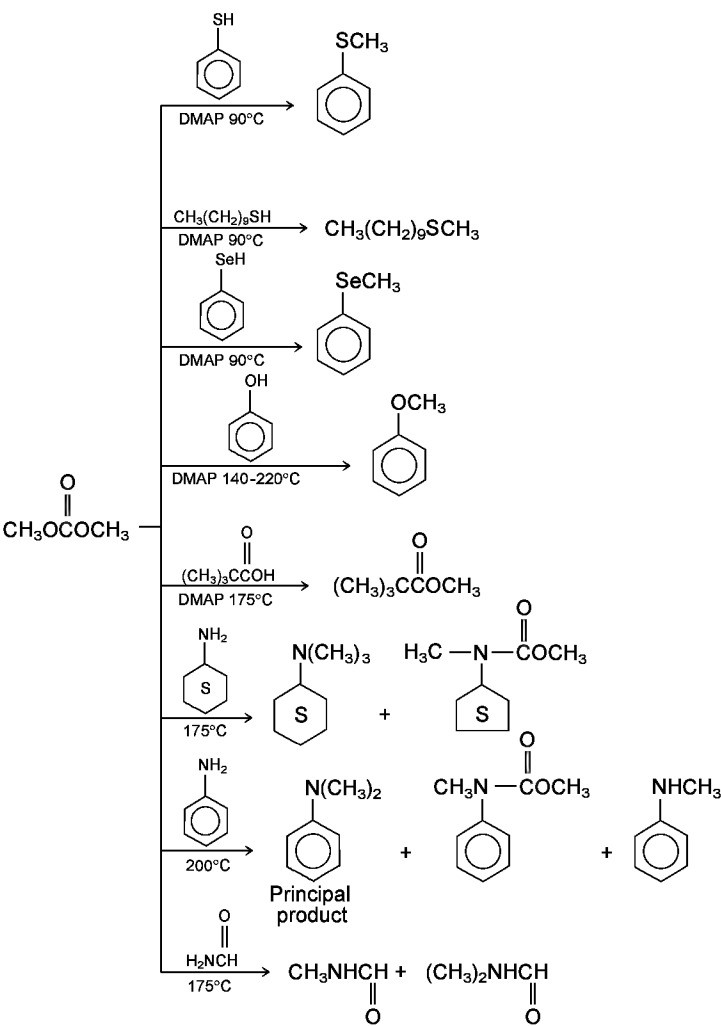


Fig. 1. Dimethyl carbonate as a methylating agent.

Manufacture

Carbonates are manufactured by essentially the same method as chloroformates except that more alcohol is required in addition to longer reaction times and higher temperatures. The products are neutralized, washed, and distilled. Corrosion-resistant equipment similar to that described for the manufacture of chloroformates is required. Diaryl carbonates are prepared from phosgene and two equivalents of the sodium phenolates or with phenols and various catalysts (76–79).

The continuous production of high purity methyl or ethyl carbonate from the alcohol and chloroformates has been patented (80). Chloroformate and alcohol are fed continuously into a Raschig ring-packed column in which a temperature gradient of 72–127°C is maintained between base and head of the column; HCl is withdrawn at the head, and carbonate (99% o) is withdrawn at the base.

In the 1990s, the trend is to manufacture carbonates without the use of phosgene. This method has the advantage of avoiding the use of highly toxic phosgene as well as considerably lower cost. A number of different processes for the manufacture of dimethyl carbonate have been patented that use methanol, CO, hydrogen, oxygen, and a variety of catalyst systems (73,81–83). The nonphosgene route has also been utilized for synthesis of aromatic carbonates (84–86) and ethylene carbonate (87,88).

Shipping and Storage

Dimethyl and diethyl carbonates are shipped in nonreturnable 208-L (55-gal) polyethylene drums with carbon steel overpack or high density poethylene drums. For bulk shipments, insulated stainless steel tank containers and trucks provide secure protection. Diethylene glycol bis(allyl) carbonate is shipped in drums as above.

The carbonates should be plainly labeled and stored in cool, dry areas away from sources of ignition. The U.S. Department of Transportation (DOT) Hazardous Materials Regulations control the shipment of carbonates as described in Table 8.

Table 8. Department of Transportation Regulations for Carbonate Shipments

Type	DOT hazard class	Tank truck	Drums
dimethyl carbonate	flammable liquid	yes	yes
diethyl carbonate	flammable liquid	yes	yes
diethylene glycol bis(allyl) carbonate	chemical NOS		yes

Economic Aspects

As in the case of the chloroformates, most of the carbonate production is used captively and production figures are not available. However, from published data, the 1991 price (fob works) of commercial carbonates was \$3.08 /kg for both dimethyl (DMC), drums, truckload and diethyl (DEC), tankwagon (89).

Specifications

Table 9 lists the specifications of the more important commercial carbonates.

Table 9. Specifications of Commercial Carbonates

Assay	Dimethyl	Diethyl	Diethylene glycol bis(allyl)
min, ° o	98	98	94
acidity, max ° o	0.02	0.02	
water, max ° o	0.2	0.10	
sp gr, 20°C 4°C	1.070–1.075	0.973–0.977	1.14–1.16
nonvolatile matter, max ° o	0.01	0.005	1.0 at 150°C ^a
boiling point, °C	90	127	
viscosity, mPa·s(– cP)	0.664 20°C	0.868 28°C	25 25°C
surface tension at 20°C, mNm (– dyn cm)		26.31	35
mol wt	90.1	118.1	274.3

^a At 0.7 kPa (– 5 mm Hg).

Health and Safety

Unlike chloroformates, diethyl and dimethyl carbonates are only mildly irritating to the eyes, skin, and mucous membranes. Diethylene glycol bis(allyl carbonate) may be irritating to the skin, but it is not classified as a toxic substance; however, it is extremely irritating to the eyes.

Protective clothing, rubber gloves, safety goggles, and adequate ventilation are recommended for all personnel handling high concentrations of carbonates. In case of fire, foam, carbon dioxide, or dry chemical extinguishing agents should be used. However, it is permissible to use a water spray to cool any drums in the vicinity, thus avoiding any spread of the fire.

Uses

Commercially, the most important carbonate has been the diethy ester. It is used in many organic syntheses, particularly of pharmaceuticals and pharmaceutical intermediates. It is also used as a solvent for many synthetic and natural resins, and in vacuum tube cathode-fixing lacquers. Dimethyl carbonate is gaining commercial importance because of its lower cost from the nonphosgene route. Dimethyl carbonate is used in the synthesis of pharmaceuticals, agricultural chemicals, dyestuffs, and as a specialty solvent. It has been used in gasoline to improve octane number (90), as a phase separation inhibitor in liquid hydrocarbon fuel and ethanol mixtures (91), and as a carbonylating and methylating agent (63–75). Dipropyl carbonate is also an organic intermediate, a specialty solvent, and is used in photoengraving as an assist agent for silicon circuiting. Ethylene carbonate is an important solvent for polymers, such as polyacrylonitrile, and may become an important raw material for synthesizing carbonates. The lower alkyl carbonates and diphenyl carbonate are used in the preparation of polycarbonate resins by transesterification (92). Diethylene glycol bis(allyl carbonate) polymerizes easily because of its two double bonds and is used for colorless, optically clear castings. Polymerization is catalyzed by the use of diisopropyl peroxydicarbonate [105-64-6] (93–95). Such polymers are used in the preparation of safety glasses, lightweight prescription lenses, glazing cast sheet, and optical cement (see ALLYL MONOMERS AND POLYMERS; POLYCARBONATES).

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Suresh B. Damle
PPG Industries, Inc.

CARBONIZATION.

See COAL CONVERSION PROCESSES, CARBONIZATION.

CARBON MONOXIDE

Carbon monoxide [630-08-0], CO, a colorless, odorless, flammable, toxic gas, is produced by steam reforming or partial oxidation of carbonaceous materials. It is used as a fuel, a metallurgical reducing agent, and a feedstock in the manufacture of a variety of chemicals, notably methanol, acetic acid, phosgene, and oxo alcohols. Increased usage of carbon monoxide from coal in chemicals and fuels manufacture is likely if economic coal gasification technology continues to evolve (see FUELS, SYNTHETIC).

Carbon monoxide was discovered in 1776 by heating a mixture of charcoal and zinc oxide. It provided a source of heat to industry and homes as a component of town gas and was used as a primary raw material in German synthetic fuel manufacture during World War II; its compounds with transition metals have been studied extensively (see CARBONYLS). Most recently, carbon monoxide emission from vehicle exhausts has been recognized as a primary source of air pollution (qv).

Physical and Thermodynamic Properties

The physical and thermodynamic properties of carbon monoxide are well documented in a number of excellent summaries (1–8). The thermochemical data cited here are drawn predominantly from references 1–3; physical property data from reference 5. A summary of particularly useful physical constants is presented in Table 1.

Table 1. Physical Properties of Carbon Monoxide

Property	Value
mol wt	28.011
melting point, K	68.09
boiling point, K	81.65
ΔH , fusion at 68 K, kJ mol ³	0.837
ΔH , vaporization at 81 K, kJ mol ^a	6.042
density at 273 K, 101.3 kPa ^b , g L	1.2501
sp gr ^c , liquid, 79 K	0.814
sp gr ^d , gas, 298 K	0.968
critical temperature, K	132.9
critical pressure, MPa ^b	3.496
critical density, g cm ³	0.3010
triple point	
temperature, K	68.1
pressure, kPa ^e	15.39
ΔG° formation at 298 K, kJ mol ³	137.16
ΔH° formation at 298 K, kJ mol ^a	110.53
S° formation at 298 K, kJ (mol·K) ^a	0.1975
C_p° at 298 K, J (mol·K) ^a	29.1
C_v° at 298 K, J (mol·K) ^a	20.8
autoignition temperature, K	882
bond length, nm	0.11282
bond energy, kJ mol ^a	1070
force constant, mN m (dyn cm)	1,902,000
dipole moment, C·m ^f	0.374×10^{-30}
ionization potential, eV	14.01
flammability limits in air ^g	
upper limit, %	74.2
lower limit, %	12.5

^a To convert J to cal, divide by 4.184.

^b 101.3 kPa = 1 atm; to convert MPa to atm, multiply by 9.87.

^c With respect to water at 277 K.

^d With respect to air at 298 K.

^e To convert kPa to torr, multiply by 7.5.

^f To convert C·m to debye, multiply by 2.99×10^{29} .

^g Saturated with water vapor at 290 K.

Values for the free energy and enthalpy of formation, entropy, and ideal gas heat capacity of carbon monoxide as a function of temperature are listed in Table 2 (1). Thermodynamic properties have been reported from 70–300 K at pressures from 0.1–30 MPa (1–300 atm) (8,9) and from 0.1–120 MPa (1–1200 atm) (10).

Table 2. Thermodynamic Data for Carbon Monoxide (Ideal Gas)^{a, b}

Temperature, K	<i>C_p</i> , J (mol·K)	ΔH_f° , kJ mol	ΔG_f° , kJ mol	<i>S</i> °, J (mol·K)
0 K	0.00	−113.80	−113.80	0.00
100 K	29.104	−112.45	−120.25	165.74
298 K	29.142	110.53	137.16	197.54
400 K	29.342	110.11	146.34	206.12
500 K	29.794	110.02	155.41	212.72
1000 K	33.183	112.01	200.24	234.42
5000 K	38.074	144.41	524.32	292.74

^a Ref. 1.

^b To convert J to cal, divide by 4.184.

Solid carbon monoxide exists in one of two allotropes, a body-centered cubic or a hexagonal structure. The body-centered structure converts into the hexagonal structure at 62 K with a heat of transition of 0.632 kJ mol (0.151 kcal mol) (5). The melting point at atmospheric pressure is 68.1 K and rises to 73 K at 20.7 MPa (205 atm) (5).

The vapor pressure of carbon monoxide has been compiled (11). Liquid-phase vapor pressure is represented by equation 1, where *P* is the pressure in MPa or atm and *T* is the temperature in K (2).

$$\log_{10} P = 4.80780 \text{ (or } 3.81341) - \frac{291.743}{T - 5.15}$$

(1)

The compressibility factor *Z* can be calculated (12) for carbon monoxide at pressures up to 8 MPa (80 atm) by equation 2.

$$Z = 1 + \frac{BP}{RT} + \frac{(C - B^2) P^2}{(RT)^2}$$

(2)

Values for *B* and *C* are listed in Table 3. An alternative equation is available (12) to extend the range of calculated compressibilities to pressures up to 300 MPa (3000 atm). Additional compressibility data over a wide range of conditions have been reported (13,14).

Table 3. Virial Coefficients for Carbon Monoxide^{a, b}

Temperature, K	<i>B</i> , cm ³ mol	<i>C</i> , cm ³ mol ²
273.16 K	14.19	1781
298.16 K	8.28	1674
323.16 K	3.40	1591
348.16 K	0.90	1444
373.16 K	4.49	1339
398.16 K	7.52	1264
423.16 K	10.04	1259

^a Ref. 12.

^b See equation 2. *R* = 8.314 (mL·MPa) (mol·K) or 82.06(mL·atm) (mol·deg).

The density of liquid carbon monoxide at various temperatures is listed in Table 4 (5,7). The density of gaseous carbon monoxide (7) can be calculated directly from the equation of state using the compressibility factor at the temperature and pressure of interest.

Table 4. Density of Liquid Carbon Monoxide^a

Temperature, K	Liquid density, g mL
68.2 K	0.847
78.1 K	0.806
87.2 K	0.769
94.2 K	0.734
103.6 K	0.685
109.1 K	0.653
121.0 K	0.566
125.7	0.521
130.0 K	0.456
131.4 K	0.422

^a Refs. 5 and 7.

Values of the viscosity of gaseous carbon monoxide have been reported (5,8,15,16). Vapor viscosity values and their relationship to density have been tabulated over a wide range of conditions (15). Values for liquid carbon monoxide may be obtained (7).

Extensive listings of thermal conductivity for liquid and gaseous carbon monoxide and relationships of thermal conductivity to pressure appear in the literature (7,17).

The solubility of carbon monoxide in a variety of solvents at 928 K is given in Table 5 (18), and a detailed discussion of the solubility of carbon monoxide in water has been provided (19). A compilation of early literature values is given (20).

Table 5. Solubility of Carbon Monoxide at 25°C and 101.3 kPa (1 atm) CO Pressure,^a mol fraction CO × 10⁴

Solvent	Solubility	Solvent	Solubility
1-heptane	17.24	chlorobenzene	6.47

cyclohexane	9.91	nitrobenzene	3.72
methylcyclohexane	12.41	methanol	3.76
benzene	6.68	ethanol	4.84
toluene	8.11	2-methyl-1-propanol	6.52
perfluoro- <i>n</i> -heptane	38.75	acetone	7.72
perfluorobenzene	21.20	water	0.16
carbon tetrachloride	8.76		

^a Ref. 18.

Carbon monoxide burns readily in air or oxygen. Ignition temperatures are 644–658°C and 637–658°C, respectively. Mixtures of carbon monoxide and air are flammable over a wide range of compositions at atmospheric pressure (Table 6) (21,22). The flammability limits of carbon monoxide–air mixtures change with pressure. As pressure increases, the lower limit rises slowly from 16.3° at 0.1 MPa (1 atm) to 20° at 2 MPa (20 atm), and remains at 20° with pressures to 20 MPa (200 atm), and the upper limit decreases, dropping from 70° at 0.1 MPa to 60° at 2 MPa and to 53° at 10 MPa (100 atm). Carbon monoxide–oxygen mixtures are flammable over a wider range than carbon monoxide–air mixtures. The lower flammability limit remains nearly the same at 16.7°, but the upper flammability limit increases to 93.5° (23). Addition of diluents, particularly carbon dioxide, decreases the range of flammability of carbon monoxide in both air and oxygen (21).

Table 6. Flammability Limits of Carbon Monoxide in Dry Air as a Function of Temperature at Atmospheric Pressure ^a

Temperature, K	Lower limit, vol %	Upper limit, vol %
290 K	16.3	70.0
373 K	14.8	71.5
473 K	13.5	73.0
573 K	12.4	75.0
673 K	11.4	77.5

^a Refs. 21,22.

Chemical Properties

According to molecular orbital theory the 10 valence electrons from carbon and oxygen in CO fill the lowest energy molecular orbitals to give the electronic configuration $(\zeta^b)^2(\zeta^*)^2(\pi^b_{xy})^4(\pi^b_z)^2$ (b , bonding; * , antibonding) which predicts one ζ - and two π -bonds (24). The π^* and ζ^* orbitals of molecular carbon monoxide remain unfilled but available for bonding with transition-metal atoms. The bond energy of 1070 kJ mol (255.7 kcal mol) is consistent with the triple-bond formulation and is the highest observed bond energy for any diatomic molecule. The fundamental absorption in the infrared spectrum of carbon monoxide is located at 2143 cm^{−1}.

The bonding between carbon monoxide and transition-metal atoms is particularly important because transition metals, whether deposited on solid supports or present as discrete complexes, are required as catalysts for the reaction between carbon monoxide and most organic molecules. A metal–carbon ζ -bond forms by overlapping of metal $d\text{-}\zeta$ orbitals with ζ orbitals on carbon. Multiple-bond character between the metal and carbon occurs through formation of a metal-to-CO π -bond by overlap of metal- $d\text{-}\pi$ orbitals with empty antibonding orbitals of carbon monoxide (Fig. 1).

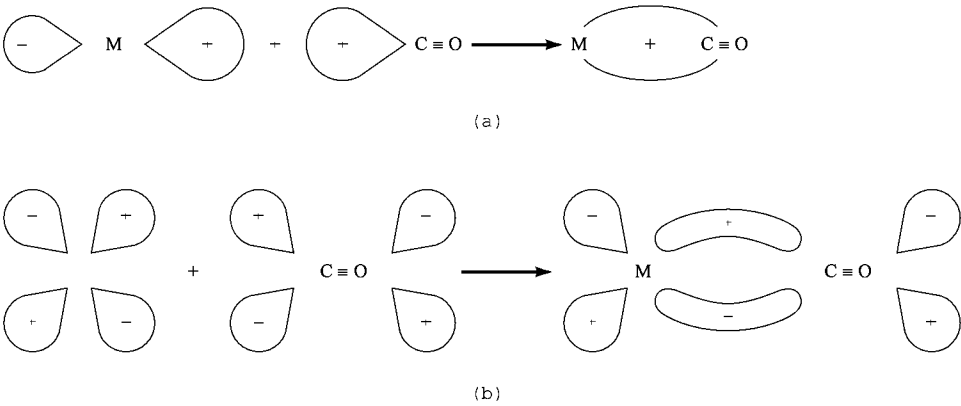
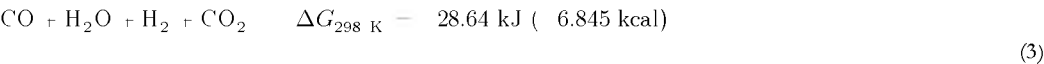


Fig. 1. (a) Formation of a ζ -bond between a transition metal and carbon monoxide. (b) Metal-to-carbon monoxide π -bond formation.

A weakened carbon–oxygen bond results from the combined ζ - and π -bonding, allowing the metal-bonded carbon monoxide to react more readily (see CARBONYLS).

INDUSTRIALLY SIGNIFICANT REACTIONS OF CARBON MONOXIDE

Conversion to Hydrogen (Water Gas Shift Reaction). Carbon monoxide reacts with water over a catalyst to produce hydrogen and carbon monoxide (25). This reaction is used to prepare high purity hydrogen or synthesis gas with a higher hydrogen-to-carbon monoxide ratio than the feed (eq. 3).



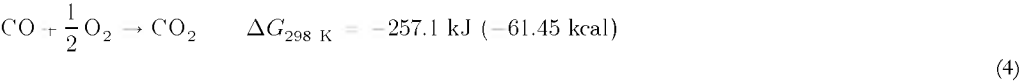
The reaction is exothermic, and its equilibrium, unaffected by pressure, favors hydrogen production as the reaction temperature is reduced (see FUELS, SYNTHETIC; HYDROGEN).

The shift reaction is carried out commercially in either a one- or two-stage catalytic process. The first stage, or high temperature shift converter, operates at 588–783 K using a long-lived, reduced iron catalyst. Exit carbon monoxide concentrations of 2–5° are obtained at space velocities of 2000–4000 h^{−1}. Water-to-carbon monoxide ratios of 2:4 are typically used to force the equilibrium toward hydrogen production. In multibed, first-stage reactors, water is sometimes added between beds to remove reaction heat and lower the gas exit temperatures to favor higher hydrogen concentrations.

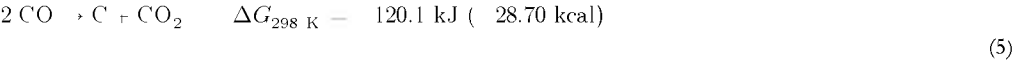
In the second stage, a more active zinc oxide–copper oxide catalyst is used. This higher catalytic activity permits operation at lower exit temperatures than the first-stage reactor, and the resulting product has as low as 0.2° carbon monoxide. For space velocities of 2000–4000 h^{−1}, exit carbon monoxide

concentrations of 0.5% are typical. After bulk carbon dioxide is removed (see CARBON DIOXIDE), residual carbon oxides are hydrogenated to methane using a reduced nickel catalyst.

Oxidation. Carbon monoxide can be oxidized without a catalyst or at a controlled rate with a catalyst (eq. 4) (26). Carbon monoxide oxidation proceeds explosively if the gases are mixed stoichiometrically and then ignited. Surface burning will continue at temperatures above 1173 K, but the reaction is slow below 923 K without a catalyst. Hopcalite, a mixture of manganese and copper oxides, catalyzes carbon monoxide oxidation at room temperature; it was used in gas masks during World War I to destroy low levels of carbon monoxide. Catalysts prepared from platinum and palladium are particularly effective for carbon monoxide oxidation at 323 K and at space velocities of 50 to 10,000 h⁻¹. Such catalysts are used in catalytic converters on automobiles (27) (see EXHAUST CONTROL, AUTOMOTIVE).



Disproportionation. Carbon monoxide readily disproportionates into elemental carbon and carbon dioxide [124-38-9] on a catalyst surface (eq. 5).



This decomposition is thermodynamically favored by decreasing temperature and increasing pressure (28). Decomposition is extremely slow below 673 K in the absence of a catalyst; however, between 673–873 K many surfaces, particularly iron (29), cobalt, and nickel (30), promote the disproportionation reaction.

Phosgene. The reaction between carbon monoxide and chlorine is catalyzed by activated carbon and gives phosgene [75-44-5] in nearly quantitative yield (eq. 6) (25).



An equimolar mixture of carbon monoxide and chlorine reacts at 500 K under a slight positive pressure. The reaction is extremely exothermic ($\Delta H_{500\text{K}} = -109.7 \text{ kJ}$ or -26.22 kcal), and heat removal is the limiting factor in reactor design. Phosgene (qv) is often produced on-site for use in the manufacture of toluene diisocyanate (see AMINES, AROMATIC DIAMINOTOLUENES; ISOCYANATES, ORGANIC).

Methanol. Methanol [67-56-1] is manufactured by the reaction between carbon monoxide and hydrogen at 503–673 K and 5–60 MPa (50–600 atm) (eq. 7).



High pressure processes ($P > 150 \text{ atm}$) are catalyzed by copper chromite catalysts. The most widely used process, however, is the low pressure methanol process that is conducted at 503–523 K, 5–10 MPa (50–100 atm), space velocities of 20,000–60,000 h⁻¹, and H₂-to-CO ratios of 3. The reaction is catalyzed by a copper–zinc oxide catalyst using promoters such as alumina (31,32). This catalyst is more easily poisoned than the older copper chromite catalysts and requires the use of sulfur-free synthesis gas.

The reaction between carbon monoxide and hydrogen is exothermic ($\Delta H_{600\text{K}} = -100.5 \text{ kJ}$ or 24.0 kcal) and plants must be designed to remove heat efficiently. In order to control the exotherm, CO conversions are typically maintained well below the equilibrium conversion, 45% at 523 K. This necessitates a substantial recycle of carbon monoxide and hydrogen.

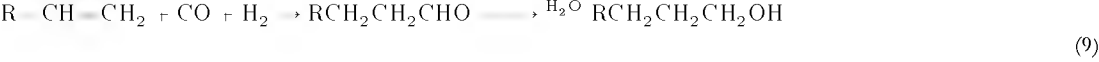
The U.S. Department of Energy has funded a research program to develop the liquid-phase methanol process (LPMEOH) (33). This process utilizes a catalyst such as copper–zinc oxide suspended in a hydrocarbon oil. The liquid phase is used as a heat-transfer medium and allows the reaction to be conducted at higher conversions than conventional reactor designs. In addition, the use of the LPMEOH process allows the use of a coal-derived, CO-rich synthesis gas. Typical reactor conditions for this process are 3.5–6.3 MPa (35–60 atm) and 473–563 K (see METHANOL).

Acetic Acid. Manufacture of acetic acid [64-19-7] by homogeneous catalytic methanol carbonylation has become the leading commercial route to acetic acid (eq. 8) (34,35).



The original catalysts for this process were iodide-promoted cobalt catalysts, but high temperatures and high pressures (493 K and 48 MPa) were required to achieve yields of up to 60% (34,35). In contrast, the iodide-promoted, homogeneous rhodium catalyst operates at 448–468 K and pressures of 3 MPa. These conditions dramatically lower the specifications for pressure vessels. Yields of 99% acetic acid based on methanol are readily attained (see ACETIC ACID; CATALYSIS).

Hydroformylation. Probably the best known catalytic carbonylation reaction is the hydroformylation, or oxo reaction, for producing aldehydes and alcohols from carbon monoxide, hydrogen, and olefins (eq. 9) (36).

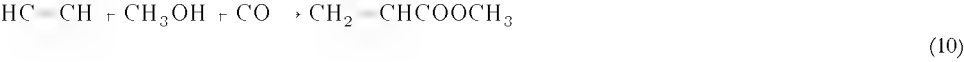


In excess of a million metric tons of oxo products are produced in the United States annually. They are used in the manufacture of plasticizers, solvents, and detergents. The principal oxo alcohol product, 2-ethyl-1-hexanol [104-76-7] is made from propylene [115-07-1] and represents about 75% of the oxo market.

The hydroformylation reaction is carried out in the liquid phase using a metal carbonyl catalyst such as HCo(CO)₄ (36), HCo(CO)₃[P(*n*-C₄H₉)] (37), or HRh(CO)₂[P(C₂H₅)₃]₂ (38,39). The phosphine-substituted rhodium compound is the catalyst of choice for new commercial plants that can operate at 353–383 K and 0.7–2 MPa (7–20 atm) (39). The differences among the catalysts are found in their intrinsic activity, their selectivity to straight-chain product, their ability to isomerize the olefin feedstock and hydrogenate the product aldehyde to alcohol, and the ease with which they are separated from the reaction medium (36).

A new homogeneous process for hydroformylation of olefins using a water-soluble catalyst has been developed (40). The catalyst is based on a rhodium complex and utilizes a water-soluble phosphine such as tri(*M*-sulfophenyl)phosphine. The use of an aqueous phase simplifies the separation of the catalyst and products (see OXO PROCESS).

Acrylic Acid. In Europe some acrylic acid [79-10-7] and ester is manufactured by the Reppe reaction from acetylene, methanol, and carbon monoxide (eq. 10) (see AACRYLIC ACID AND DERIVATIVES).



The reaction is carried out in the liquid phase at 373–463 K and 3 MPa (30 atm) of carbon monoxide pressure using nickel salt catalyst, or at 313 K and 0.1 MPa (1 atm) using nickel carbonyl as both the catalyst and the source of carbon monoxide. Either acrylic acid or methyl acrylate may be produced directly, depending on whether water or methanol is used as solvent (41). New technology for acrylic acid production uses direct propylene oxidation rather than acetylene carbonylation because of the high cost of acetylene. This new process has completely replaced the old in the United States (see

ACETYLENE DERIVED CHEMICALS).

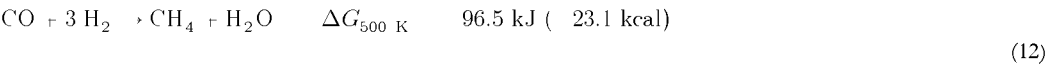
Fischer-Tropsch. Carbon monoxide is catalytically hydrogenated to a mixture of straight-chain aliphatic, olefinic, and oxygenated hydrocarbon molecules in the Fischer-Tropsch reaction (eq. 11) (see FUELS, SYNTHETIC).



The Fischer-Tropsch process was developed in Germany to manufacture synthetic gasoline during World War II. Carefully promoted iron and cobalt catalysts operating at conditions varying from 463–623 K and 0.7–20 MPa (7–200 atm) were used. Depending on the specific operating conditions, products containing up to 75% liquid hydrocarbon or 55% oxygenated organic molecules were obtained (42,43).

Although the Fischer-Tropsch reaction was the focus of innumerable studies prior to 1960, it received little further attention until the energy crisis of the 1970s spurred new activity in the area. A particularly significant technology resulting from this work was a process for converting synthesis gas or methanol into aromatic compounds (44,45). The Fischer-Tropsch synthesis is carried out commercially in South Africa, where an unusual economic environment allows a profitable operation. Fischer-Tropsch technology has not found application in the United States (46).

Methanation. Since 1902, when Sabatier discovered that carbon monoxide could be hydrogenated to methane [74-82-8] the methanation reaction (eq. 12) has been the subject of intense investigation (47,48) (see HYDROCARBONS, C₁-C).



The methanation reaction is carried out over a catalyst at operating conditions of 503–723 K, 0.1–10 MPa (1–100 atm), and space velocities of 500–25,000 h⁻¹. Although many catalysts are suitable for effecting the conversion of synthesis gas to methane, nickel-based catalysts are used almost exclusively for industrial applications. Methanation is extremely exothermic ($\Delta H_{500\text{ K}} = -214.6\text{ kJ or } -51.3\text{ kcal}$), and heat must be removed efficiently to minimize loss of catalyst activity from metal sintering or reactor plugging by nickel carbide formation.

The methanation reaction is currently used to remove the last traces (<1%) of carbon monoxide and carbon dioxide from hydrogen to prevent poisoning of catalysts employed for subsequent hydrogenation reactions. Processes for conversion of synthesis gas containing large quantities of carbon monoxide (up to 25%) into synthetic natural gas have been investigated to serve plants based on coal-supplied synthesis gas.

Nickel Purification. The Mond process for nickel purification is based on the formation of volatile nickel carbonyl, Ni(CO)₄, which is stable below 60°C but decomposes rapidly and completely into nickel and carbon monoxide at 453 K. Crude nickel oxide, obtained from roasting nickel sulfide ores, is reduced to impure nickel metal with synthesis gas at 673 K. Under these conditions the reduction is carried out by hydrogen alone. Water is then removed and the exit gas, enriched in carbon monoxide, passes over the impure nickel at 50°C to form nickel carbonyl. The volatile nickel carbonyl [13463-39-3] leaves the reactor and is decomposed at 180°C, pure nickel is deposited on nickel shot, and the carbon monoxide is recycled for the preparation of additional carbonyl (49).

GENERAL REACTIONS OF CARBON MONOXIDE

With Hydrogen. In addition to the reactions already discussed, other products may be obtained from synthesis gas depending on the catalyst used. In a liquid-phase high pressure reaction (60 MPa or 600 atm), a rhodium cluster complex catalyzes the direct formation of ethylene glycol, propylene glycol (see GLYCOLS), and glycerol (qv) from synthesis gas (eq. 13) (50). Mixtures of methanol, ethanol (51), acetaldehyde, and acetic acid (52) are formed by using supported rhodium catalysts at 598 K and 17 MPa (168 atm). Rates of reaction for this latter route appear to be too slow for commercial application.

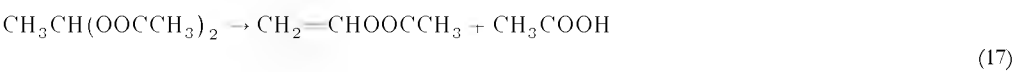
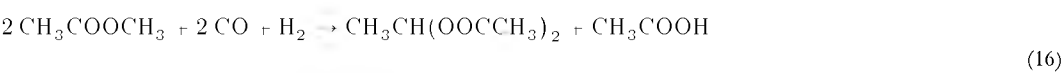
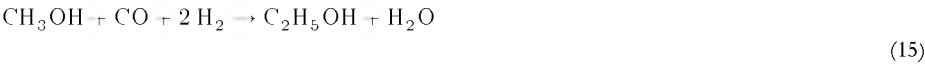


With Alcohols, Ethers, and Esters. Carbon monoxide reacts with alcohols, ethers, and esters to give carboxylic acids. The reaction yielding carboxylic acids is general for alkyl (53) and aryl alcohols (54). It is catalyzed by rhodium or cobalt in the presence of iodide and provides the basis for a commercial process to acetic acid.

Strong base catalyzes the formation of derivatives of formic acid in the reaction between alcohols and carbon monoxide (55). Methyl formate [107-31-3] is made at 443–463 K and 1–2 MPa (10–20 atm) (eq. 14).



Methanol reacts with carbon monoxide and hydrogen to form ethanol in the homologation reaction. Cobalt carbonyl catalyzes the transformation at 473 K and 30 MPa (300 atm) pressure, and gives yields of less than 75% ethanol. The greatest activity in the homologation reaction is observed for methyl and benzyl alcohols (eq. 15) (56). Reaction between methyl acetate, carbon monoxide, and hydrogen at 408–433 K and up to 10 MPa (100 atm) pressure using a palladium or rhodium iodide catalyst leads to the production of ethylidene diacetate (57) (eq. 16). Ethylidene diacetate [542-10-9] can be pyrolyzed to vinyl acetate [108-05-4] (eq. 17) (see VINYL POLYMERS).



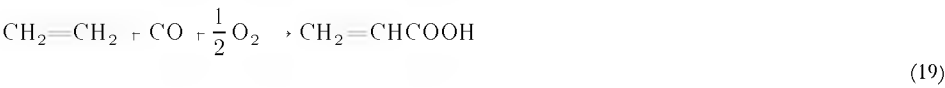
With Formaldehyde. The sulfuric acid catalyzed reaction of formaldehyde [50-00-0] with carbon monoxide and water to glycolic acid [79-14-1] at 473 K and 70 MPa (700 atm) pressure was the first step in an early process to manufacture ethylene glycol [107-21-1]. A patent (58) has described the use of liquid hydrogen fluoride as catalyst, enabling the reaction to be carried out at 298 K and 7 MPa (70 atm) (eq. 18).



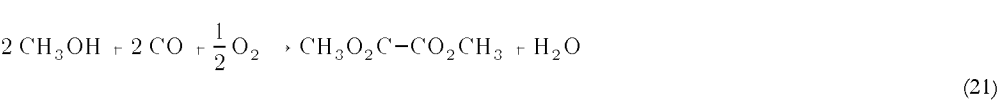
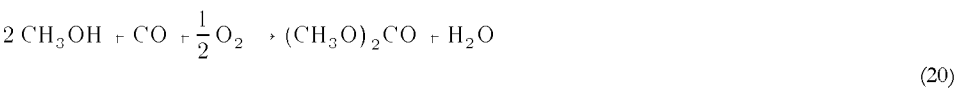
With Unsaturated Compounds. The reaction of unsaturated organic compounds with carbon monoxide and molecules containing an active hydrogen atom leads to a variety of interesting organic products. The hydroformylation reaction is the most important member of this class of reactions. When the hydroformylation reaction of ethylene takes place in an aqueous medium, diethyl ketone [96-22-0] is obtained as the principal product instead of propionaldehyde [123-38-6] (59). Ethylene, carbon monoxide, and water also yield propionic acid [79-09-4] under mild conditions (448–468 K and 3–7 MPa or 30–70 atm) using cobalt or rhodium catalysts containing bromide or iodide (60,61).

Carbon monoxide also reacts with olefins such as ethylene to produce high molecular weight polymers. The reaction of CO with ethylene can be initiated by an x-ray irradiator (62) or transition-metal catalyzed reactions (63). The copolymerization of ethylene with carbon monoxide is catalyzed by cationic Pd (II) complexes such as {Pd[P(C H₅)₃]_n(CH₃CN)_{4-n}} (BF₄)₂ where n = 1–3. With this catalyst, copolymerization can be carried out at 25°C and pressures as low as 2.1 MPa.

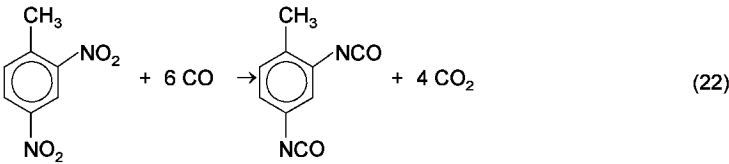
Oxidative Carbonylation. Carbon monoxide is rapidly oxidized to carbon dioxide; however, under proper conditions, carbon monoxide and oxygen react with organic molecules to form carboxylic acids or esters. With olefins, unsaturated carboxylic acids are produced, whereas alcohols yield esters of carbonic or oxalic acid. The formation of acrylic and methacrylic acid is carried out in the liquid phase at 10 MPa (100 atm) and 110°C using palladium chloride or rhenium chloride catalysts (eq. 19) (64,65).



Dimethyl carbonate [616-38-6] and dimethyl oxalate [553-90-2] are both obtained from carbon monoxide, oxygen, and methanol at 363 K and 10 MPa (100 atm) or less. The choice of catalyst is critical; cuprous chloride (66) gives the carbonate (eq. 20); a palladium chloride–copper chloride mixture (67,68) gives the oxalate, (eq. 21). Anhydrous conditions should be maintained by removing product water to minimize the formation of by-product carbon dioxide.



Isocyanate Synthesis. In the presence of a catalyst, nitroaromatic compounds can be converted into isocyanates, using carbon monoxide as a reducing agent. Conversion of dinitrotoluene into toluenediisocyanate (TDI) with carbon monoxide (eq. 22), could offer significant commercial advantages over the current process using phosgene. The reaction is carried out at 473–523 K and 27–41 MPa (270–400 atm) with a catalyst consisting of either palladium chloride or rhodium chloride complexed with pyridine, isoquinoline, or quinoline and yields are in excess of 80% TDI (69,70).

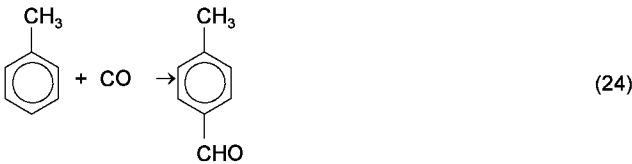


Dimethylformamide. The industrial solvent dimethylformamide [68-12-2] is manufactured by the reaction between carbon monoxide and dimethylamine [124-40-3].



The reaction is carried out in the liquid phase using a sodium methoxide catalyst at 60–130°C and 0.5–0.9 MPa (5–9 atm) (71).

Aromatic Aldehydes. Carbon monoxide reacts with aromatic hydrocarbons or aryl halides to yield aromatic aldehydes (see ALDEHYDES). The reaction of equation 24 proceeds with yields of 89% when carried out at 273 K and 0.4 MPa (4 atm) using a boron trifluoride–hydrogen fluoride catalyst (72), whereas conversion of aryl halides to aldehydes in 84% yield by reaction with CO + H₂ requires conditions of 423 K and 7 MPa (70 atm) with a homogeneous palladium catalyst (73) and also produces HCl.



Metal Carbonyls. Carbon monoxide forms metal carbonyls or metal carbonyl derivatives with most transition metals (74) (see COORDINATION COMPOUNDS). Metal carbonyls are used in a variety of industrial applications in addition to their use as catalysts. Methylcyclopentadienylmanganesetricarbonyl (MMT), [CH₃C₅H₄Mn(CO)₃] was sold as an antiknock additive, but its use in unleaded gasoline was banned by the Environmental Protection Agency (EPA) in 1978; tungsten and molybdenum hexacarbonyls are thermally decomposed to obtain very pure metal films; and numerous carbonyls are used as reagents in organic synthesis (see CARBONYLS).

Polymerization. Carbon monoxide forms copolymers with ethylene and suitable vinyl compounds. No large-scale uses for the copolymers or their further reaction products such as polyalcohols and polyamines have been found (75).

Analysis

Many procedures for the analysis of carbon monoxide have been developed based on the reducing properties of the gas (76,77). Qualitative detection of carbon monoxide is achieved by passing the gas through palladium chloride that is either in solution or impregnated on paper. Appearance of black metallic palladium is an indication of the presence of carbon monoxide. Using this technique, concentrations of 100–1000 ppm carbon monoxide in air are easily estimated. Hydrogen, hydrogen sulfide, ethylene, and acetylene also reduce PdCl₂ to palladium, interfering with quantitative determination of carbon monoxide.

Several quantitative procedures for concentrations above 0.1 vol % are available. Gas chromatographic analysis (78) is particularly useful because it is fast, accurate, and relatively inexpensive. The standard wet-chemical, analytical method (76) takes advantage of the reaction between iodine pentoxide and carbon monoxide at 423 K.

A variety of instruments are available to analyze carbon monoxide in gas streams from 1 ppm to 90%. One group of analyzers determines the concentration of carbon monoxide by measuring the intensity of its infrared stretching frequency at 2143 cm⁻¹. Another group measures the oxidation of carbon monoxide to carbon dioxide electrochemically. Such instruments are generally lightweight and well suited to applications requiring portable analyzers. Many analyzers are equipped with alarms and serve as work area monitors.

Manufacture and Purification

Of the four commercial processes for the purification of carbon monoxide two processes are based on the absorption of carbon monoxide by salt solutions, the third uses either low temperature condensation or fractionation, and the fourth method utilizes the adsorption of carbon monoxide on a solid adsorbent material. All four processes use similar techniques to remove minor impurities. Particulates are removed in cyclones or by scrubbing. Scrubbing also removes any tars or heavy hydrocarbon fractions. Acid gases are removed by absorption in monoethanolamine, hot potassium carbonate, or by other patented removal processes. The purified gas stream is then sent to a carbon monoxide recovery section for final purification and by-product recovery.

The selection of a separation process depends on many factors, not the least of which is the type of gas to be purified. Table 7 gives some

compositions of typical gases obtained using standard commercial production techniques.

Table 7. Typical Analyses of Carbon Monoxide Sources^a

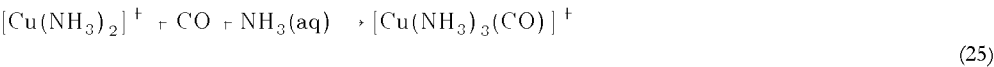
Source	Composition, vol % , dry basis					
	CO	CO ₂	H ₂	N ₂	CH ₄	Other
blast furnace gas	27.5	11.5	1.0	60.0		
coke oven gas ^b	5.6	1.4	55.4	4.3	28.4	4.5
water gas ^c	30.0	3.4	31.7	13.1	12.2	8.4
natural gas, steam reforming	15.5	8.1	75.7	0.2	0.5	
naphtha, steam reforming	6.7	15.8	65.9	2.6	6.3	2.7
partial oxidation, heavy fuel oil	47.0	5.5	4.0	0.3	0.1	0.1
coal gasification	59.4	10.0	29.4	0.6		0.6

^a Refs. 79–82.
^b Also, 0.4 vol % O₂.
^c Also, 1.2 vol % O₂.

The carbon monoxide concentration of gas streams is a function of many parameters. In general, increased carbon monoxide concentration is found with an increase in the carbon-to-hydrogen ratio in the feed hydrocarbon; a decrease in the steam-to-feed-carbon ratio; increase in the synthesis gas exit temperature; and avoidance of reequilibration of the gas stream at a temperature lower than the synthesis temperature. Specific improvement in carbon monoxide production by steam reformers is made by recycling by-product carbon dioxide to the process feed inlet of the reformer (83,84). This increases the relative carbon-to-hydrogen ratio of the feed and raises the equilibrium carbon monoxide concentration of the effluent.

Some gas streams contain nitrogen. In these cases it is difficult to achieve high carbon monoxide purity by cryogenic methods because the boiling points of nitrogen and carbon monoxide differ by only 2 K. Therefore, when the nitrogen content of the feed gas exceeds the product purity specification, a salt solution absorption process is preferred for purification. If high purity carbon monoxide and hydrogen are required, the cryogenic processing route is favored because salt solution processes cannot independently purify the hydrogen stream. As noted earlier, gas composition and system application are primary factors in the selection of a carbon monoxide purification route.

Copper–Liquor Scrubbing. Cuprous ammonium salts of organic acids form complexes with carbon monoxide.



Conditions of high pressure and low temperature favor the formation of the complex, whereas low pressure and high temperature tend to release the complexed carbon monoxide from solution. These conditions typify the operation of the absorber-stripper shown in Figure 2. Specific design conditions for the process are given in references 86–88, and an excellent summary of processing considerations is presented in reference 85.

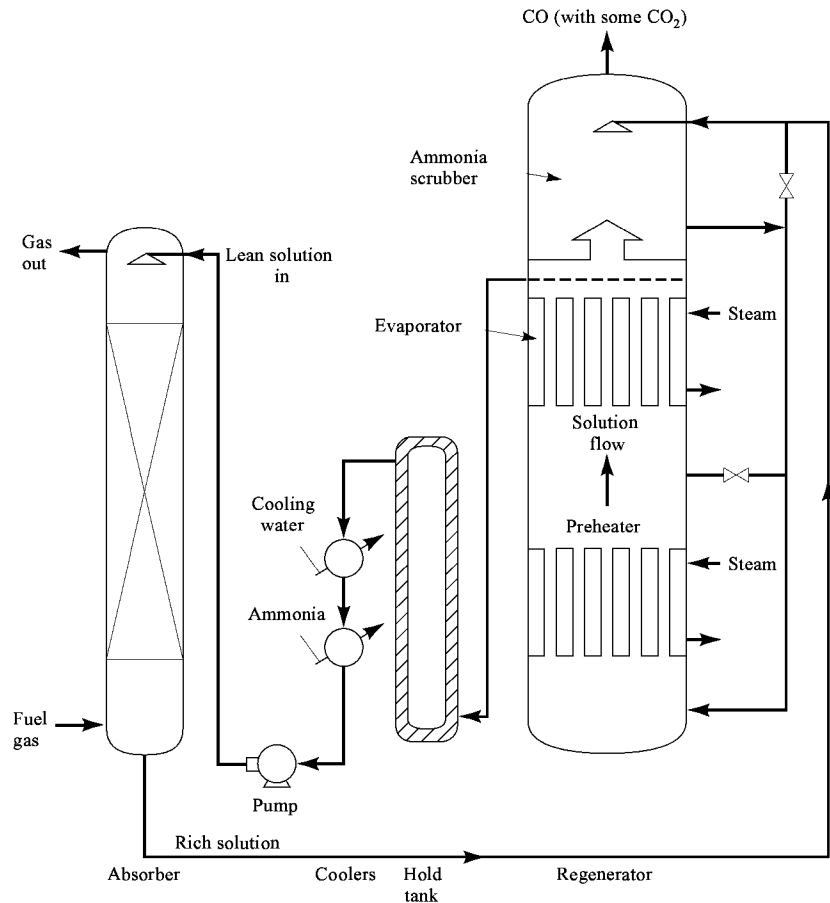


Fig. 2. Copper–ammonium salt processes (85).

Courtesy of Gulf Publishing Co.

Because the solution is capable of absorbing one mole of carbon monoxide per mole of cuprous ion, it is desirable to maximize the copper content of the solution. The ammonia not only complexes with the cuprous ion to permit absorption but also increases the copper solubility and thereby permits an even greater carbon monoxide absorption capacity. The ammonia concentration is set by a balance between ammonia vapor pressure and solution acidity. Weak organic acids, eg, formic, acetic, and carbonic acid, are used because they are relatively noncorrosive and inexpensive. A typical formic acid

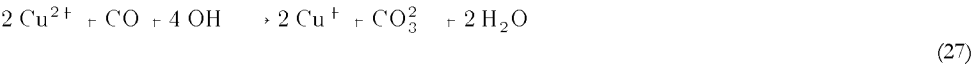
solution analysis (85) is Cu⁺, 170 g L; Cu²⁺, 25 g L; HCOOH, 110 g L; CO₂, 60 g L; and NH₃, 140 g L. This type of solution can absorb between 3 and 20 volumes (STP) of carbon monoxide per volume of solution depending on process conditions. High carbon monoxide partial pressures and low solution temperatures favor high absorption coefficients.

The preferred ratio of cuprous to cupric ion ranges from 5:1 to 10:1, depending on system conditions. Too high a concentration of cuprous ion causes the system to disproportionate and form metallic copper (eq. 26):



Cupric ion concentration is kept at an acceptable but low level by direct air oxidation of the solution. Solids formation from sulfides in the feed gas is also possible; therefore, pretreatment for sulfur removal is required.

Carbon dioxide can cause product contamination through ammonium carbonate formation. Ammonium carbonate may also form by oxidation of carbon monoxide by cupric ion (eq. 27):



In both cases, the carbonate ion concentration increases and eventually equilibrates in the system, releasing carbon dioxide in the stripping column and thereby reducing product purity. Hence, a small caustic wash tower is employed to remove any carbon dioxide that is liberated in the stripper.

A small quantity of ammonia vapor is always in equilibrium with the solution. Losses of ammonia from the absorber are negligible owing to the high absorption pressure and the low operating temperature, usually 2.5 MPa (25 atm) and 283–303 K. The greatest potential for ammonia loss comes in the regenerator, where a pressure of 0.1 MPa (1 atm) is typical and stripping temperatures often reach 80°C. The loss is minimized by washing the product gas with the relatively cold saturated solution from the absorber.

Cryogenic Purification. Both the partial condensation process and absorption in liquid methane operate at cryogenic temperatures and elevated pressures and rely on the expansion energy in the feed gas to produce most or all of the refrigeration energy required (see CRYOGENICS). Process selection depends on product purity specifications for both the carbon monoxide and hydrogen streams. The partial condensation technique is employed to produce carbon monoxide and moderate purity grades of hydrogen (96–98%). The carbon monoxide purity is dictated by the feed impurities, typically methane, which exit with the carbon monoxide. If a higher purity-grade of carbon monoxide (99%) is required, an absorption system is used subsequent to the partial condensation unit. A liquid methane scrubbing system is generally applied when high purity standards are set for the hydrogen stream. This technique can produce hydrogen at a purity of 99+ % with less than 1 ppm of carbon monoxide (89). High purity levels of carbon monoxide (99+ %) can also be obtained.

As in the case of the salt complexation processes, the cryogenic systems require prepurification of the feed gas. Bulk water, hydrogen sulfide, and carbon dioxide are removed by standard techniques. Final removal of these materials is accomplished by adsorption. After prepurification, the gases are ready for cryogenic processing.

In the partial condensation system, the feed gas is cooled from ambient temperature to approximately 85 K by heat exchange with the exit gases (Fig. 3). Cooling condenses the bulk carbon monoxide contained in the feed as well as all of the methane. The uncondensed hydrogen-rich gas stream is removed overhead for further processing. The liquid fraction is then lowered in pressure to remove entrained gases. The low pressure, carbon monoxide-rich, liquid stream is evaporated, warmed against the incoming feed gas, compressed, and leaves the processing area as the carbon monoxide product. Because there are only two process exit streams, the bulk of the inlet feed contaminants, mainly methane and nitrogen, leave with the carbon monoxide product.

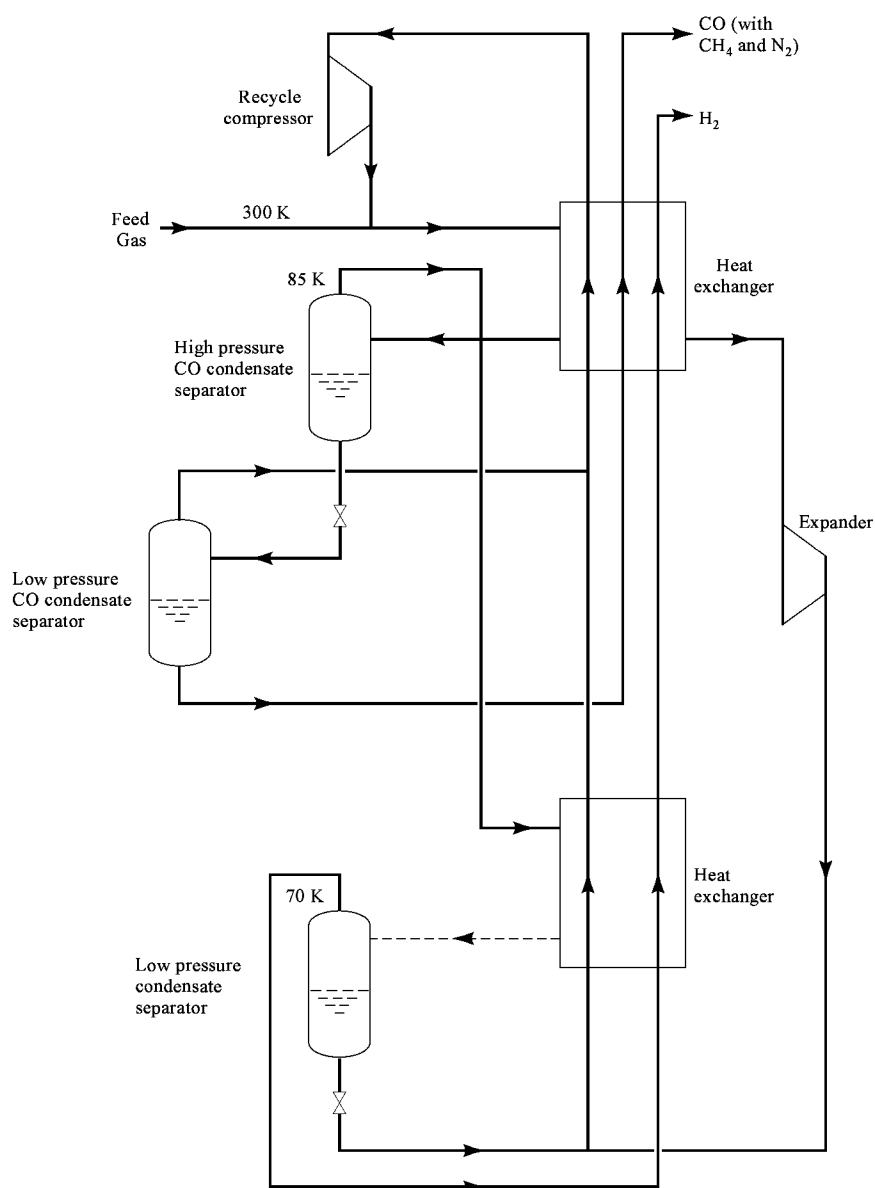


Fig. 3. Cryogenic partial condensation process (89).

Courtesy of Linde AG.

The hydrogen-rich gas from the high pressure separator is cooled to about 70 K in a second exchanger. This allows additional carbon monoxide and other inlet gases to be condensed and separated from the hydrogen product stream. Hydrogen purities in excess of 95% are usually obtained. The hydrogen is warmed serially against the low temperature and raw-feed gas streams and exits the process at high pressure. Typically, a portion of this gas stream is expanded to provide the lowest temperature refrigeration for the system. The expanded hydrogen and low temperature condensate streams are warmed against the raw hydrogen stream, then combined with the vent gas from the low pressure CO-condensate separator, and heat-exchanged with the feed gas. The mixture is recompressed and recycled to the feed stream.

The processing techniques employed for the methane wash process are more complex but produce a higher purity carbon monoxide than those employed by the partial condensation system. In the methane wash process, the inlet gas is cooled to about 90 K in a series of heat exchangers (Fig. 4). Bulk carbon monoxide is removed by condensation in a separator, and the hydrogen stream is sent to the methane wash column where it is purified by scrubbing with a liquid methane reflux. The liquor absorbs the carbon monoxide and other gases and carries them to a second column. The purified hydrogen is heat-exchanged against the incoming gas and is available for use at high pressure. A portion of this gas stream is expanded to provide energy for refrigeration. This hydrogen stream is removed from the system and is available as a low pressure hydrogen product.

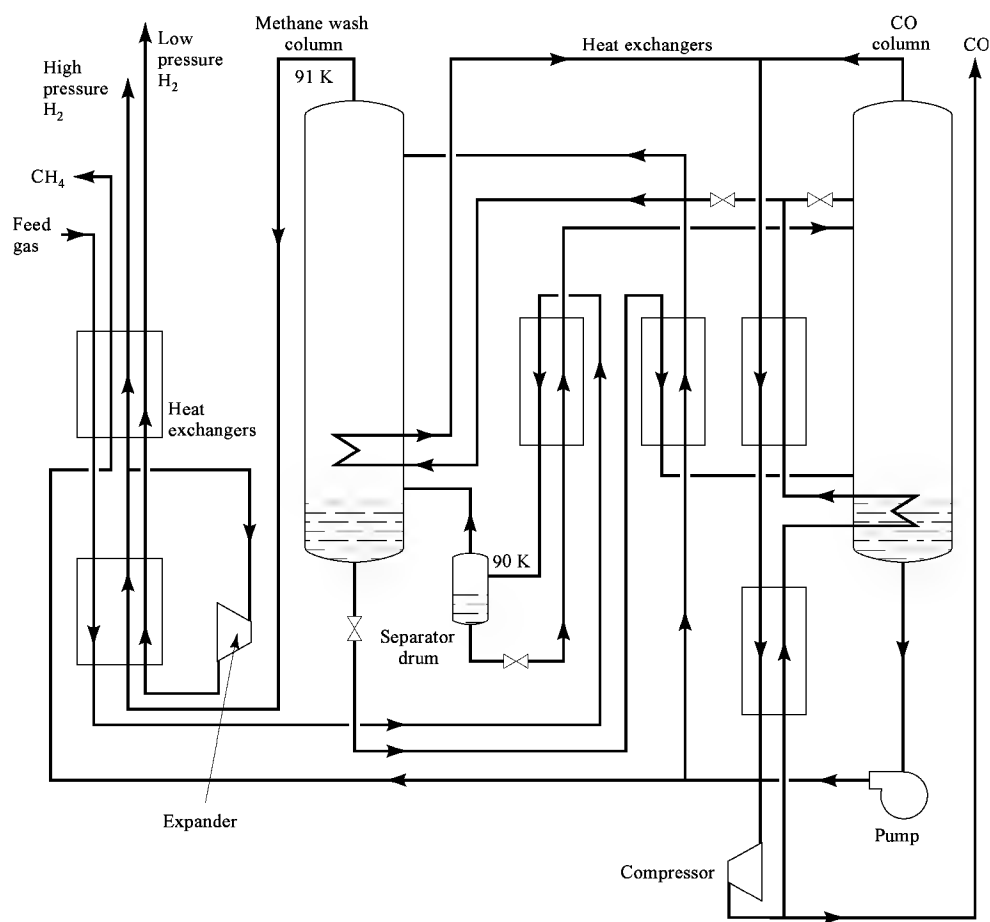


Fig. 4. Liquid methane wash process (89).

Courtesy of Linde AG.

The carbon monoxide-rich, liquid condensate from the primary separator is expanded and exchanged against the incoming feed and is then sent to a distillation column where the carbon monoxide is purified. The bottoms liquor from the methane wash column is expanded, heat-exchanged, and sent to the bottom section of the distillation column for methane rectification and carbon monoxide recovery. The methane bottom stream is recompressed and recycled to the top of the wash column after subcooling. A sidestream of methane is withdrawn to avoid a buildup of impurities in the system.

The carbon monoxide product is removed from the top of the column and warmed against recycled high pressure product. The warm low pressure stream is compressed, and the bulk of it is recycled to the system for process use as a reboiler medium and as the reflux to the carbon monoxide column; the balance is removed as product. The main impurity in the stream is nitrogen from the feed gas. Carbon monoxide purities of 99.8% are commonly obtained from nitrogen-free feedstocks.

Cosorb Process. Like the copper-liquor scrubbing method, the Cosorb process also relies on the formation of a cuprous complex of carbon monoxide but uses a nonaqueous organic solvent. The preferred system uses a cuprous tetrachloroaluminate toluene complex in a toluene solvent (90). Many other organometallic complex variants have been proposed (91–93) but have not been commercialized.

The main advantages of the Cosorb process over the older copper ammonium salt process are low corrosion rate, ability to work in carbon dioxide atmospheres, and low energy consumption. The active $\text{CuAlCl}_4 \cdot \text{C}_6\text{H}_5\text{CH}_3$ complex is considerably more stable than the cuprous ammonium salt, and solvent toluene losses are much lower than the ammonia losses of the older process (94).

A flow diagram for the system is shown in Figure 5. Feed gas is dried, and ammonia and sulfur compounds are removed to prevent the irreversible buildup of insoluble salts in the system. Water and solids formed by trace ammonia and sulfur compounds are removed in the solvent maintenance section (96). The pretreated carbon monoxide feed gas enters the absorber where it is selectively absorbed by a countercurrent flow of solvent to form a carbon monoxide complex with the active copper salt. The carbon monoxide-rich solution flows from the bottom of the absorber to a flash vessel where physically absorbed gas species such as hydrogen, nitrogen, and methane are removed. The solution is then sent to the stripper where the carbon monoxide is released from the complex by heating and pressure reduction to about 0.15 MPa (1.5 atm). The solvent is stripped of residual carbon monoxide, heat-exchanged with the stripper feed, and pumped to the top of the absorber to complete the cycle.

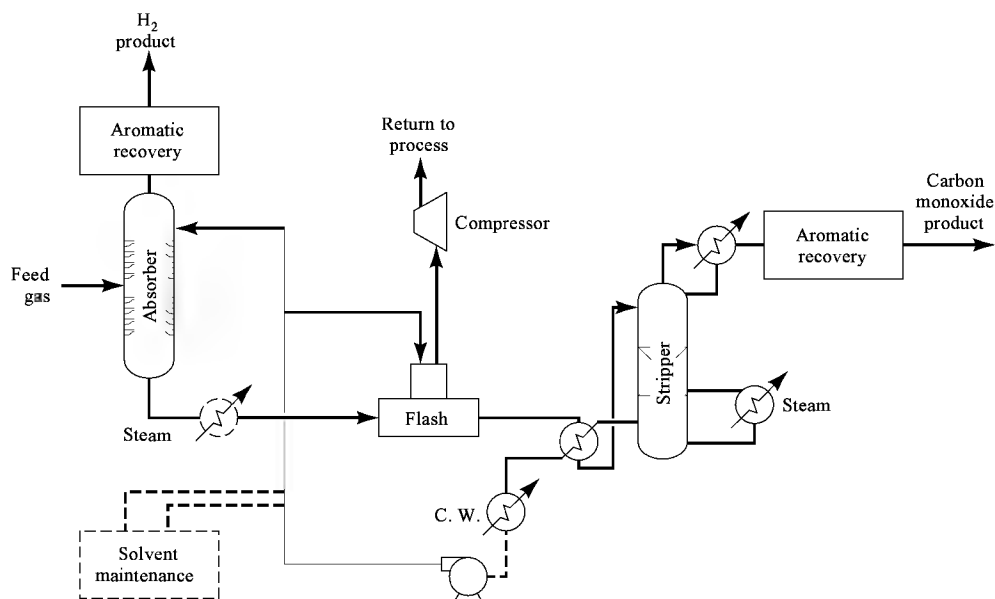


Fig. 5. Cosorb process (95).

The overhead temperatures of both the absorber and stripper are kept as low as possible to minimize solvent carryover. A temperature of about 311 K is typically used in the high pressure absorber. The overhead temperature in the stripper is set by the boiling point of the saturated complex solution and by the operating pressure of the stripper. At a stripping pressure of 0.166 MPa (1.7 atm), a temperature of 378 K is used. The solvent-rich gas from the stripper is cooled to recover as much solvent as possible by condensation prior to the final aromatics-recovery section. Final solvent recovery is accomplished by adsorption on activated carbon (95).

The carbon monoxide purity from the Cosorb process is very high because physically absorbed gases are removed from the solution prior to the low pressure stripping column. Furthermore, there is no potential for oxidation of absorbed carbon monoxide as in the copper-liquor process. These two factors lead to the production of very high purity carbon monoxide, 99+ %. Feed impurities exit with the hydrogen-rich tail gas; therefore, the purity of this coproduct hydrogen stream depends on the impurity level in the feed gas.

The high degree of carbon monoxide recovery (99+ %) is enhanced as absorption pressure is increased. The solution circulation rate is kept low by maximizing the concentration of cuprous complex in solution, eg, 25 wt % CuAlCl₄ · C₂H₅CH₃ in toluene. Solution temperatures must be controlled to prevent solids formation at these high concentrations. Lack of water in the system coupled with low corrosivity of the solvent system allows the use of high stripper-bottoms temperatures that permit generation of a solution with a very low residual concentration of the carbon monoxide complex. The high carbon monoxide absorption rate of the resulting solution contributes to the excellent monoxide recovery in the system. The low corrosion rate also allows the use of carbon steel equipment throughout the process.

Adsorption Processes. More recently, pressure swing adsorption (PSA) processes utilizing a high selectivity copper adsorbent have been utilized to effectively separate carbon monoxide from blast furnace gas and coke oven gas (97–101).

In these processes, a carbon monoxide containing gas is fed to an adsorber bed containing copper, typically dispersed on a high surface area support such as alumina or carbon. The copper is present predominately as Cu⁺, which selectively adsorbs carbon monoxide. The remainder of the gas stream passes through the adsorbent bed. The carbon monoxide is then removed from the adsorbent by lowering the pressure. Figure 6 shows a typical process for a CO-PSA process. Process conditions are typically adsorption pressures of 0.68–204 MPa (6.8–20.4 atm) and temperatures of 313–373 K. Regeneration occurs at reduced pressure or by vacuum.

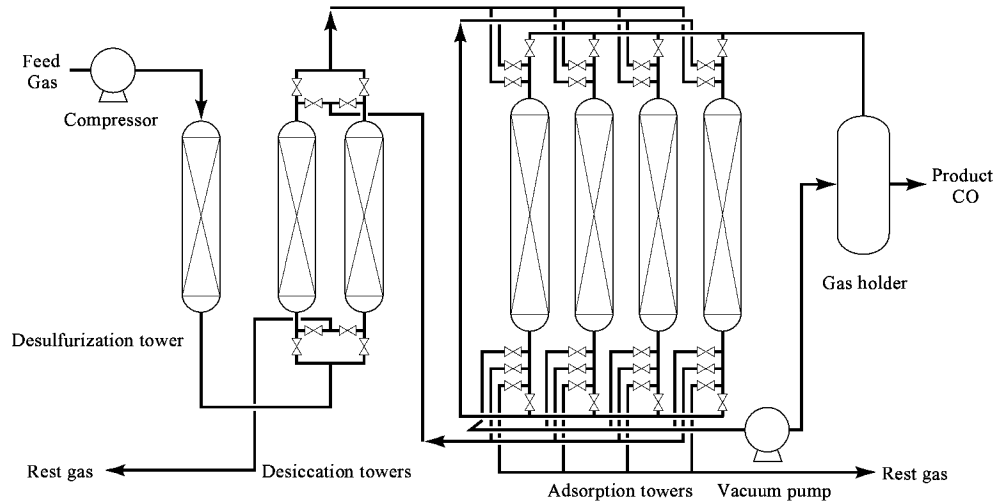


Fig. 6. CO-PSA process flow (99).

Economic Aspects

Carbon monoxide is produced as a component of synthesis gas or as purified gas by many manufacturers, primarily for on-site process applications. Because very few producers engage in merchant sale of purified gases, published production data are not available. By-product hydrogen price, feedstock prices, and delivery charges as well as location, purity, and volume affect carbon monoxide pricing. The following prices are illustrative of carbon monoxide derived from typical steam-methane reformer operations for a current Gulf Coast location. Prices range from \$0.29 to \$0.32 m³, (\$8 to \$9 1000 scf) for volumes of approximately 28,000 m³ day (1 million scfd) for "over the fence" carbon monoxide, to \$1.42 m³ (\$40 1000 scf) for tube trailer volumes of gas, fob works. Tube trailers generally haul loads of 1500 to 3000 m³ (50,000 to 100,000 scf). Purchases of liquefied carbon monoxide are possible through some vendors; however, volume and availability are restricted. Gas volumes are based on equivalent volumes at 0.101 MPa (1 atm) and 21.1°C.

Carbon monoxide is also available in cylinders at various levels of purity. As in the case of bulk gas sales, price is also a function of delivery location, cylinder size, and purity. Terminology for gas purity has not been standardized by the Compressed Gas Association; thus care must be taken when comparing grades from different suppliers. Table 8 contains the price ranges and purities from supplier catalog data (102–104). The price ranges quoted are for the largest available cylinders in each grade provided by the vendor. All prices are quoted fob vendor works. Carbon monoxide must bear a red label during shipment because it is flammable. Additional shipping requirements are contained in the Interstate Commerce Commission regulations.

Table 8. Commercial Price and Purity Data for Cylinder Carbon Monoxide^a

Grade	Purity, min vol %	Supply pressure, MPa ^b	Cylinder price, \$ /cylinder	Gas price, ^c \$ /m ³
commercial	98.0–99.0	11.5–13.9	62–102	15.27–36.40
CP	99.0–99.5	11.5–13.9	35–145	21.71–40.00
ultrahigh purity	99.8	11.5	312	63.03
research	99.97–99.99	11.5	45–337	67.94–1580

^a Refs. 101–103.
^b To convert MPa to psig, multiply by 145, then subtract 14.7.
^c Gas volumes are based on equivalent volume at 0.101 MPa (1 atm) and 21.1°C.

Health and Safety

Occurrence. Carbon monoxide is a product of incomplete combustion and is not likely to result where a flame burns in an abundant air supply, yet may result when a flame touches a cooler surface than the ignition temperature of the gas. Gas or coal heaters in the home and gas space heaters in industry have been frequent sources of carbon monoxide poisoning when not provided with effective vents. Gas heaters, though properly adjusted when installed, may become hazardous sources of carbon monoxide if maintained improperly. Automobile exhaust gas is perhaps the most familiar source of carbon monoxide exposure. The manufacture and use of synthesis gas, calcium carbide manufacture, distillation of coal or wood, combustion operations, heat treatment of metals, fire fighting, mining, and cigarette smoking represent additional sources of carbon monoxide exposure (105–107).

Toxicity. Carbon monoxide is the most widely spread gaseous hazard to which humans are exposed (105). The toxicity of carbon monoxide is a result of its reaction with the hemoglobin of blood. The carboxyhemoglobin (COHb) that is formed displaces oxygen and leads to asphyxiation. Blood levels of COHb as low as 5% impair the function of the brain and reduce visual acuity. Headaches occur when 10–20% of the hemoglobin reacts with carbon monoxide. Increased saturation causes nausea, dizziness, weakness, mental confusion, loss of consciousness, and death. In cases of severe poisoning, the skin and mucous membranes may become cherry red, but the victim usually appears pale (106). Prolonged unconsciousness may result in permanent brain damage. There is little evidence of chronic poisoning from repeated exposure to low concentrations of carbon monoxide. However, because of associated oxygen deprivation, repeated exposure may result in persistent neurologic manifestations such as anorexia, headache, dizziness, and ataxia (106).

The recommended NIOSH limit of 35 ppm is the time-weighted average exposure to carbon monoxide based on a carboxyhemoglobin level of 5%; this amount of COHb is what an employee engaged in sedentary activity would be expected to approach in eight hours of continuous exposure. The standard does not take into account the smoking habits of a worker; the level of COHb in chronic cigarette smokers has generally been found to be in the 4–5% range prior to carbon monoxide exposure (105). A concentration of 100 ppm is allowable for an exposure of several hours and 400–500 ppm can be inhaled for one hour without an appreciable effect, whereas 1500–2000 ppm are dangerous and 4000 ppm or more is fatal (106). First aid treatment for carbon monoxide poisoning emphasizes elimination of the gas from the body. Elimination of carbon monoxide occurs solely through the lungs, and though rapid at first, the last traces are difficult to remove. The poisoned patients must be removed to fresh air, kept warm, and administered pure oxygen by the best method available. Artificial respiration is necessary whenever breathing is inadequate. Exercise and stimulants, including carbon dioxide, must not be given because they can lead to collapse. A physician must be summoned in all cases of suspected carbon monoxide poisoning (107).

Prevention of carbon monoxide poisoning is best accomplished by providing good ventilation where contamination is a problem. If good ventilation is not possible, a self-contained breathing apparatus, such as a Scott Air-Pak, must be used. The use of gas masks containing an adsorbent is generally not recommended since it is difficult to know when the adsorbent is exhausted.

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CARBON MONOXIDE–HYDROGEN REACTIONS.

See FUELS, SYNTHETIC.

CARBONYLS

Carbon monoxide [630-08-0] (qv), CO, the most important π -acceptor ligand, forms a host of neutral, anionic, and cationic transition-metal complexes. There is at least one known type of carbonyl derivative for every transition metal, as well as evidence supporting the existence of the carbonyls of some lanthanides (qv) and actinides (1) (see ACTINIDES AND TRANSACTINIDES; COORDINATION COMPOUNDS).

Carbonyls are useful in the preparation of high purity metals as in the Mond process for the extraction of nickel from its ores (see NICKEL AND NICKEL ALLOYS), in catalytic applications, and in the synthesis of organic compounds. Metal carbonyls are employed in the preparation of complexes where the carbon monoxide ligand is replaced by halides, hydrogen, Group 15 (VA) and 16 (VIA) derivatives, arenes, and many chelating ligands (see CHELATING AGENTS). Metal carbonyls and their derivatives are suited for mechanistic studies under favorable experimental conditions. Substitution rates on some metal carbonyls such as those of Cr, Mo, W, and Mn can be easily measured (2). Detailed mechanistic studies on metal carbonyls have become increasingly important in understanding the factors influencing ligand substitution processes, especially as they apply to catalytic activity. Cluster complexes containing several metal atoms held together mainly by metal–metal bonding have received increasing attention for the interest in the rules governing the stoichiometry and structure as well as for possibilities in homogeneous and heterogeneous catalysis (qv). Transition-metal carbonyls of the type $M_x(CO)_y$, where M is a metal in the zero oxidation state and x and y are integers are discussed herein.

Structure and Bonding of Metal Carbonyls

Numerous theoretical approaches have been used in predicting and describing the bonding and structure of metal carbonyls. The Sidgwick concept of effective atomic number, or the 18-electron rule, has been particularly useful in predicting formulas, and molecular orbital and ligand field calculations have provided additional insight to the more detailed features of bonding in metal carbonyls.

Bonding. The 18-electron rule requires that each metal interact with a sufficient number of CO molecules and additionally in polynuclear complexes, ie, those containing more than one metal atom, with sufficient neighboring metal atoms to allow the metal to achieve the electronic structure of the subsequent inert gas in the periodic table. Each CO is counted as supplying a pair of electrons either in a terminal (*T*) or in a bridging (*B*) position, whereas neighboring metal atoms in polynuclear carbonyls each contribute one electron through a metal–metal bond of bond order 1. In some special cases, bridging carbonyls interacting both through the carbon as well as the oxygen of the CO group (μ,η^2 -CO) contribute four electrons. These bonding modes are shown in Figure 1.

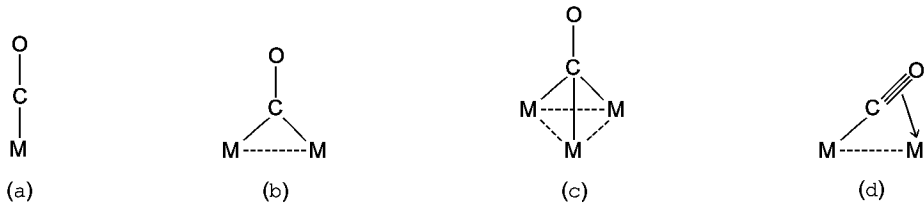


Fig. 1. Bonding modes of CO: (a), terminal (*T*), (b), doubly bridged (*B*); (c), triply bridged (*B*); and (d), the (μ,η^2 -) entity.

For example, in $Ni(CO)_4$ nickel metal having 28 electrons coordinates four CO molecules to achieve a total of 36 electrons, the configuration of the inert gas krypton. Nearly every metal forming a carbonyl obeys the 18-electron rule. An exception is vanadium, forming a hexacarbonyl in which the number of electrons is 35. This carbonyl, which has a paramagnetism equivalent to one unpaired electron, however, readily adds one electron to form a closed valence shell complex containing the $V(CO)_6^-$ anion.

Many metals having an odd number of electrons achieve the inert gas configuration by forming a covalent metal–metal bond or by the CO molecules acting as bridges between two metals where each metal receives one electron from each CO molecule. In some complexes, a CO molecule forms a bridge among three metal centers in which CO is still counted as a two-electron donor (Fig. 1). Carbon monoxide may also serve as a four-electron donor as in the μ,η^2 -group in the complex $(CO)_2Mn(C_6H_5)_2PCH_2CH_2P(C_6H_5)_2(\mu,\eta^2-CO)Mn(CO)_2$ (3).

The accepted view of the bonding in terminally bonded, metal carbonyl groups (*T*) is one in which charge is donated from the ligand to the metal (M) by a sigma bond and charge from the metal *d*-orbitals is back-donated into the π^* , ie, unoccupied antibonding, orbitals of the ligand. The electron density in the π -orbitals of the ligand is dependent to a certain extent on the charge donation from the ligand to the metal, therefore the ζ - and π -bonding is synergistic (Fig. 2) (6–14).

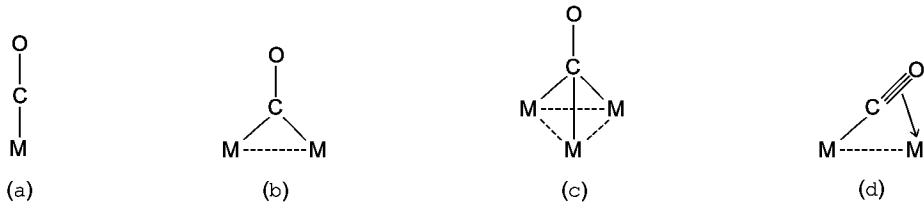


Fig. 2. Overlapping of the metal, M, *d*-orbitals with the ζ -bonding and π^* (antibonding) orbitals in a terminally bonded M–CO interaction (*T*).

Bond lengths and infrared spectra support the multiple-bond character of the M–CO bonds. Coordination of a CO molecule to a metal center can change the C–O bond order. According to the description of ζ - and π -bonding given herein, increased ζ -bonding between a metal and CO results in a

decreased bond order for the C–O bond. Increased π -bonding results in more electron density occupying the π^* orbitals of CO and hence a decrease in the C–O bond order. Changes in the bond order of C–O are reflected in the shifts of the C–O stretching frequencies in the infrared spectrum of a particular metal carbonyl. As the bond order increases, the C–O stretching frequencies shift to higher energies. Compared to the stretching frequency of free CO (2143 cm⁻¹), terminal carbonyl groups in neutral metal complexes have stretching frequencies in the range of 2125–1900 cm⁻¹, showing a reduction in the bond order of CO upon coordination. A qualitative assessment of π -back-bonding can be made by changing the electron density on the central metal and noting the change in the C–O stretching frequencies. Assuming the ζ bond remains fairly constant (4), any change in the electron density of the metal atom should result in an increase or decrease of electron density flowing through the $d\text{-}\pi$ -bonding orbitals. As the negative charge in the central metal atom is increased, the π^* orbitals of CO must accept more electron density, hence the C–O bond order should decrease. Such a trend is observed in the compounds Mn(CO)⁺, Cr(CO)₃, and V(CO)₃ where the C–O stretching frequencies decrease in the order given as the negative charge on the central metal increases (5).

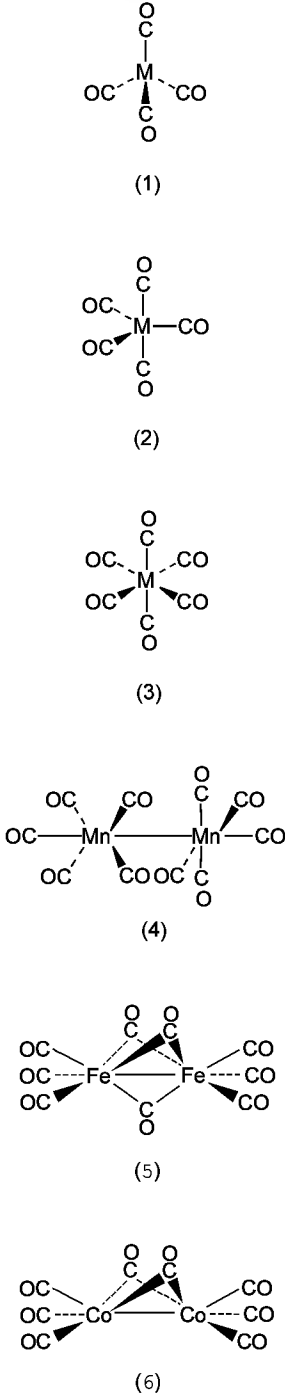
Structure. The CO molecule coordinates in the ways shown diagrammatically in Figure 1. Terminal carbonyls are the most common. Bridging carbonyls are common in most polynuclear metal carbonyls. As depicted, metal–metal bonds also play an important role in polynuclear metal carbonyls. The metal atoms in carbonyl complexes show a strong tendency to use all their valence orbitals in forming bonds. These include the nd^5 , $(n + 1)s$ and the $(n + 1)p^3$ orbitals. As a result, use of the 18-electron rule is successful in predicting the structure of most metal carbonyls.

Mononuclear Carbonyls. The lowest coordination number adopted by an isolable metal carbonyl is four. The only representative of this class is nickel carbonyl [13463-39-3], the first metal carbonyl isolated (15). The molecule possesses tetrahedral geometry as shown in structure (1). A few transient four-coordinate carbonyls, such as Fe(CO)₄, have also been detected (16).

Representative pentacarbonyls are restricted to the iron, ruthenium, and osmium group. All three pentacarbonyls possess trigonal bipyramidal structures as shown in structure (2). The pentacarbonyls of ruthenium and osmium are thermally unstable. Osmium pentacarbonyl [16406-49-8] rapidly polymerizes at room temperature to form polynuclear species. The transient species Cr(CO)₅ (17), Mo(CO)₅ (18), and W(CO)₅ (19) have been investigated.

The neutral complexes of chromium, molybdenum, tungsten, and vanadium are six-coordinate and the CO molecules are arranged about the metal in an octahedral configuration as shown in structure (3). Vanadium carbonyl possesses an unpaired electron and would be expected to form a metal–metal bond. Steric hindrance may prevent dimerization. The other hexacarbonyls are diamagnetic.

Polynuclear Carbonyls. Several structures consist of dinuclear metal carbonyls as shown in structures (4)–(6). The metal atoms in Mn₂(CO)₁₀, as also for technetium and rhenium, are held together by a metal–metal bond and the compound contains 10 terminal CO ligands, five coordinated to each atom. The CO ligands of Mn₂(CO)₁₀ adopt a staggered configuration as illustrated in structure



(4). In Fe₂(CO)₉, three CO molecules act as bridging ligands between two iron atoms as shown in structure (5). The structure of Co₂(CO)₈ (6) in the solid

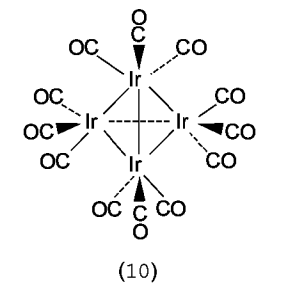
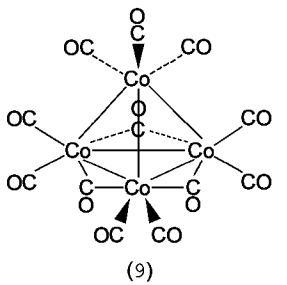
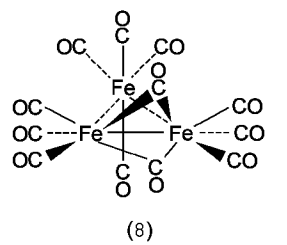
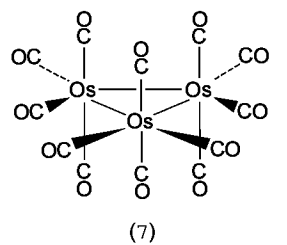
state is similar to that of $\text{Fe}_2(\text{CO})_9$ with one less bridging CO ligand.

A great many complexes of nuclearity of three and higher have been discovered since the early 1970s. Many of these contain two or more different metals, other ligands in addition to CO, and heteroatoms such as hydrogen, carbon, sulfur, or phosphorus associated with the cluster. Some are also charged as exemplified by the 42-atom cluster anions $[\text{HNi}_8\text{Pt}(\text{CO})_{48}]^5-$; and $[\text{H}_2\text{Ni}_8\text{Pt}(\text{CO})_{48}]^{4-}$; (20). Cluster complexes of nuclearity up to five or six may be termed "electron precise" (21); that is, the lines of connectivity between metal atoms represent localized two-center two-electron bonds. In higher nuclearity cluster complexes, bonding electrons are delocalized over several metal centers and suitable delocalized bonding schemes are required to describe the bonding network (21).

For trinuclear cluster complexes, open (chain) or closed (cyclic) structures are possible. Which cluster depends for the most part on the number of valence electrons, 50 in the former and 48 in the latter. The 48-valence electron complex $\text{Os}_3(\text{CO})_{12}$ is observed in the cyclic (D_{3h}) structure (7). The molecule possesses a triangular arrangement of osmium atoms with four terminal CO ligands coordinated in a *cis*-octahedral array about each osmium atom. The molecule $\text{Ru}_3(\text{CO})_{12}$ is also cyclic and is isomorphous with the osmium analogue.

The determination of the structure of $\text{Fe}_3(\text{CO})_{12}$ proved to be a difficult problem. An early report on the crystal structure claimed the molecule was a monoclinic prism and established the molecular formula (22). In a later report structure (8) was shown to be a triangular array of iron atoms with two bridging and 10 terminal CO molecules. This accepted structure was initially deduced from an x-ray crystal structure of the $\text{Fe}_3(\text{CO})_{11}\text{H}$; analogue (23).

For tetranuclear cluster complexes, three structure types are observed: tetrahedral; open tetrahedral (butterfly); or square planar, for typical total valence electron counts of 60, 62, and 64, respectively. The earliest tetracarbonyl cluster complexes known were $\text{Co}_4(\text{CO})_{12}$, and the rhodium and iridium analogues. The



60-valence electron tetranuclear complex $\text{Co}_4(\text{CO})_{12}$ contains a tetrahedral array of cobalt atoms and three bridging and nine terminal CO ligands, as shown in structure (9). The structure in solution was reported to have four bridging CO ligands (24). The rhodium analogue has the same structure as the cobalt complex. The iridium analogue (10) has no bridging ligands, but 12 terminal CO ligands coordinated equivalently among four iridium atoms.

Heteronuclear Carbonyls and High Nuclearity Carbonyl Clusters

A few of the heteronuclear metal carbonyls that have been reported are presented in Table 1. In most cases the structures of the heteronuclear species are similar to their homonuclear analogues; (11) is a notable exception (39) $[\text{Hg}_3\text{Co}_3(\text{CO})_9]\text{-}\mu\text{-Hg}_3[\text{Hg}_3\text{Co}_3(\text{CO})_9]$ [100851-89-6].

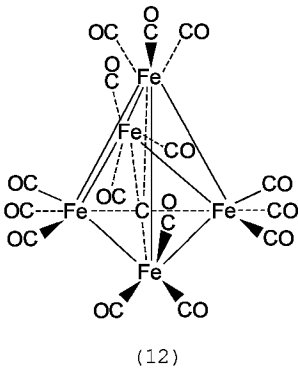
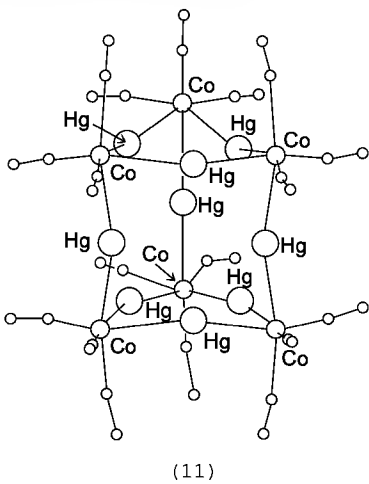
Table 1. Heteronuclear Metal Carbonyls

Heteronuclear carbonyl	CAS Registry Number	References
$(\text{CO})_5\text{MnCo}(\text{CO})_4$	[35646-82-3]	25,26
$(\text{CO})_5\text{MnRe}(\text{CO})_5$	[14693-30-2]	27
$[(\text{CO})_5\text{Mn}]_2\text{Fe}(\text{CO})_4$	[15668-57-2]	28
$[(\text{CO})_5\text{Mn}][(\text{CO})_5\text{Re}][(\text{CO})_4\text{Fe}]$	[33958-72-4]	29

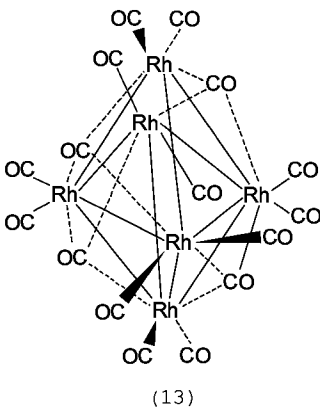
$(\text{CO})_5\text{ReCo}(\text{CO})_4$	[52647-10-6]	30
$[(\text{CO})_5\text{Re}]_2\text{Fe}(\text{CO})_4$	[16040-31-6]	31
$\text{Ru}_2\text{Os}(\text{CO})_{12}$	[12389-47-8]	32
$\text{Fe}_2\text{Ru}(\text{CO})_{12}$	[32311-57-2]	33
$\text{Zn}[\text{Mn}(\text{CO})_5]_2$	[21686-75-9]	34
$\text{Os}(\text{CO})_4[\text{Mn}(\text{CO})_5]_2$	[33292-90-9]	35
$\text{Os}(\text{CO})_4[\text{Re}(\text{CO})_5]_2$	[33153-70-7]	35
$\text{Co}_2(\text{CO})_7[\text{ZnCo}(\text{CO})_4]_2$	[93085-18-8]	36
$[\text{CoCu}(\text{CO})_4]_4$	[89462-34-0]	37
$[\text{Hg}_3\text{Co}_3(\text{CO})_9]\text{-}\mu\text{-Hg}_3[\text{Hg}_3\text{Co}_3(\text{CO})_9]$	[100851-89-6]	38
$\text{Re}_2(\text{CO})_8[\mu\text{-TiRe}(\text{CO})_5]_2$	[82025-30-7]	39

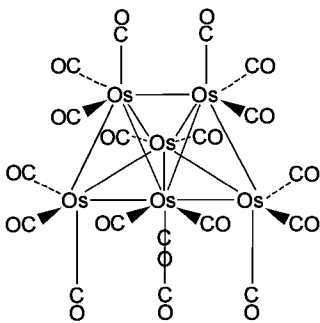
Syntheses, crystallization, structural identification, and chemical characterization of high nuclearity clusters can be exceedingly difficult. Usually, several different clusters are formed in any given synthetic procedure, and each compound must be extracted and identified. The problem may be compounded by the instability of a particular molecule. In 1962 the structure of the first high nuclearity carbide complex formulated as $\text{Fe}_5(\text{CO})_{15}\text{C}$ [11087-47-1] was characterized (40,41); see structure (12). This complex was originally prepared in an extremely low yield of 0.5%. This molecule was the first carbide complex isolated and became the forerunner of a whole family of carbide complexes of square pyramidal structure and a total of 74-valence electrons (see also CARBIDES, SURVEY).

In 1943 the reaction of anhydrous RhCl_3 and CO at 80°C under pressure with a halide acceptor, such as copper, was reported to produce a black crystalline product formulated as $\text{Rh}_4(\text{CO})_{11}$ (42). The correct structure of the complex was



determined to be $\text{Rh}_4(\text{CO})_{11}$ (43). This complex has been thoroughly studied and can be considered the forerunner of high nuclearity chemistry. The rhodium atoms are arranged at the corners of an octahedron with two terminal CO ligands coordinated to each rhodium atom. The molecule has four bridging CO molecules, each coordinated to three rhodium atoms and occupying four of the eight faces of the octahedron in structure (13). Counting nine-valence electrons for each Rh atom, and two-cluster valence electrons from each terminally bonded or face-bonded carbonyl group, a total of 86-valence electrons is achieved. An electron precise cluster, in which each edge of the octahedron represented a localized two-





(14)

center two-electron bond between adjacent metals, would only require a total of $14 \times 6 = 84$ valence electrons. The octahedral cluster $\text{Rh}(\text{CO})_6$ thus represents the first member of a family of polyhedra having triangular faces exclusively (deltahedra) in which the skeletal cluster bonding is delocalized and departs from the electron precise description (21).

Despite the complexity of transition-metal clusters, a basic structural unit is common. A triangular network of metal atoms occurs in most clusters (44). An example of a triangulated polyhedron is the molecule $\text{Os}(\text{CO})_{18}$ (45) shown in structure (14). This is a bicapped tetrahedral geometry having a total of 84 valence electrons, $(6 \times 8) + (18 \times 2)$, and is representative of the known group of 84-valence electron cluster compounds. The large cluster $[\text{Rh}_{12}(\text{CO})^{2-}_{30}]$ contains two octahedral arrays of rhodium atoms connected by a rhodium–rhodium bond and two bridging CO ligands (46). In the complexes $[\text{Co}(\text{CO})^2_{15}]$ and $[\text{Co}(\text{CO})^{4-}_{14}]$, deformation of the octahedral framework toward a trigonal prism occurs (47,48). Further twisting of the trigonal prism occurs in the dianions of $[\text{Pt}_3(\text{CO})^2_{12}]_n$; ($n = 2, 3, 4, 5$) where the structure is a twisted prism composed of layers of $\text{Pt}_3(\text{CO})$ units (49,50).

In the families of heptanuclear clusters, two geometries are found: the capped octahedron that is typical for 98-valence electrons, and the vertex-sharing open tetrahedral (butterfly) structures typical for 106-valence electrons. An example of the former is $\text{Os}_7(\text{CO})_{21}$ (51); an example of the latter is $[\text{H}_2\text{AuOs}(\text{CO})_{20}]$ (52). In the AuOs cluster anion, the gold atom is at the vertex-sharing position.

The octanuclear cluster, $[\text{Co}_8(\text{CO})_{18}\text{C}]^{2-}$, contains eight cobalt atoms in a distorted square antiprism (53). This is the best known of three possible geometries for 114-valence electron complexes. Illustrations of the high nuclearity metal clusters are given in a review (54). A survey of structural and bonding aspects in metal cluster complexes, including discussions of the higher nuclearity clusters containing up to 42 metal atoms in the $\text{Ni}_{38}\text{Pt}^{4-}$ anion, is available (55). Physical properties of some of the metal carbonyls discussed are summarized in Table 2.

Table 2. Physical Properties of Metal Carbonyls

Name	CAS Registry Number	Molecular formula	Color (solid)	Melting point, °C	Boiling point, °C ^a	M–M distances, nm	References
vanadium hexacarbonyl	[14024-00-1]	$\text{V}(\text{CO})_6$	blue-green	50 dec	40–50 ² sub		56
chromium hexacarbonyl	[13007-92-6]	$\text{Cr}(\text{CO})_6$	white	149–155	70–75 ² sub		57
molybdenum hexacarbonyl	[13939-06-5]	$\text{Mo}(\text{CO})_6$	white	150–151 dec			57
tungsten hexacarbonyl	[14040-11-0]	$\text{W}(\text{CO})_6$	white	169–170	50 sub		57
decacarbonyldimanganese	[10170-69-1]	$\text{Mn}_2(\text{CO})_{10}$	yellow	151–155	50 ^{0 001} sub	0.293	58
decacarbonylditechnetium	[14837-15-1]	$\text{Tc}_2(\text{CO})_{10}$	white	159–160	40 ^{0 001} sub	0.3036	59
decacarbonyldirhenium	[14285-68-8]	$\text{Re}_2(\text{CO})_{10}$	white	177	60 ^{0 001} sub	0.302	58
iron pentacarbonyl	[13463-40-6]	$\text{Fe}(\text{CO})_5$	white	20	103		60–62
diiron nonacarbonyl	[15321-51-4]	$\text{Fe}_2(\text{CO})_9$	yellow	100 dec		0.2523	63
triiron dodecacarbonyl	[12088-65-2]	$\text{Fe}_3(\text{CO})_{12}$	green-black	140 dec	60 ^{0 01} sub	0.263 ^b	64,65
dodecacarbonyltriruthenium	[15243-33-1]	$\text{Ru}_3(\text{CO})_{12}$	orange	150 dec		0.2848	66
dodecacarbonyltriosmium	[15696-40-9]	$\text{Os}_3(\text{CO})_{12}$	yellow	224		0.288	67,68
dicobaltoctacarbonyl	[10210-68-1]	$\text{Co}_2(\text{CO})_8$	orange	50–51	45 ^{0 1} sub	0.2542	69
tri-μ-carbonylnonacarbonyltetracobalt	[17786-31-1]	$\text{Co}_4(\text{CO})_{13}$	black	60 dec		0.249	70,71
tri-μ-carbonylnonacarbonyltetrarhodium	[19584-30-6]	$\text{Rh}_4(\text{CO})_{13}$	red	dec		0.275 ^b	71,72
hexadecacarbonylhexarhodium	[28407-51-4]	$\text{Rh}_6(\text{CO})_{16}$	black	220 dec		0.2776	43
tri-μ-carbonylnonacarbonyltetrairidium	[11065-24-0]	$\text{Ir}_4(\text{CO})_{12}$	yellow	210 dec		0.268	73
nickel carbonyl	[13463-39-3]	$\text{Ni}(\text{CO})_4$	white	25	43		74

^a Bp is at 101.3 kPa unless otherwise noted in superscript. To convert kPa to torr, multiply by 7.5.

^b Value given is average value.

Physical Properties

Most metal carbonyls are volatile solids that sublime easily. The volatility of metal carbonyls coupled with their toxicity is an important safety consideration. The vapor pressure of many metal carbonyls have been tabulated elsewhere (75).

The thermodynamic properties of simple metal carbonyls have been compiled (76–82). Some selected properties are listed in Table 3.

Table 3. Heats of Combustion and Formation for Metal Carbonyls

Molecular formular	Heat of combustion ^a , kJ mol ^b	Reference	Heat of formation, kJ mol ^b	Reference
Cr(CO)	1854	77	1077	77
Mo(CO)	2123	77	982.4	77
W(CO)	2250	77	950.6	77
Mn ₂ (CO) ₁₀	3251	79	1677	79
Fe(CO) ₅	1619	78	964.0	78
Ni(CO) ₄	1181	76	622.2	82

^a Determined for the combustion to metal oxides in the presence of oxygen.

^b To convert J to cal, divide by 4.184.

Preparation

Since the discovery of nickel carbonyl in 1890 (15), carbonyls of many other metals have been prepared. Nickel and iron are the only metals that combine directly with CO to produce carbonyls in reasonable yields. At least one carbonyl derivative is known for every *d*-block metal. A number of the neutral complexes that have been reported are listed in Table 4.

Table 4. Metal Carbonyls of the Transition Elements

Group						
4(IVB)	5(VB)	6(VIB)	7(VIIB)	8(VIII)	9(VIII)	10(VIII)
Ti(CO) ^a [61332-66-9]	V(CO) [14024-00-1]	Cr(CO) [13007-92-6]	Mn ₂ (CO) ₁₀ [10170-69-1]	Fe(CO) ₅ [13463-40-6] Fe ₂ (CO) ₉ [15321-15-4] Fe ₃ (CO) ₁₂ [12088-65-2]	Co ₂ (CO) ₈ [10210-68-1] Co ₄ (CO) ₁₂ [17786-31-1] Co (CO) ₁ ^b [12182-17-1]	Ni(CO) ₄ [13463-39-3]
	Nb(CO) ; ^c	Mo(CO) [13939-06-5]	Tc ₂ (CO) ₁₀ [14837-15-1]	Ru(CO) ₅ [16406-48-7] Ru ₃ (CO) ₁₂ [15243-33-1]	Rh ₄ (CO) ₁₂ [19584-30-6] Rh (CO) ₁ [28407-51-4]	Pd ^d
	Ta(CO) ; ^c [67290-38-0]	W(CO) [14040-11-0]	Re ₂ (CO) ₁₀ [14285-68-8]	Os(CO) ₅ ^e [16406-49-8] Os ₂ (CO) ₉ ^e [28411-13-4] Os ₃ (CO) ₁₂ [15696-40-9] Os ₅ (CO) ₁ ^h [37190-55-9] Os (CO) ₁₈ ⁱ [37216-50-5] Os ₇ (CO) ₂₁ ^h [37190-64-0] Os ₈ (CO) ₂₃ ^h [37190-66-2]	Ir ₄ (CO) ₁₂ [11065-24-0] Ir (CO) ₁ ^g [56801-74-2]	[Pt ₃ (CO)] ² ; _n ^e , [63993-21-5] n = 1 or 6 ^{c, f}

^a Matrix isolated (83).

^b Ref. 84.

^c Exists only as anions (85).

^d All attempts to synthesize this carbonyl have led to reduction to palladium metal.

^e Decomposes near room temperature (86).

^f Ref. 87.

^g Ref. 88.

^h Ref. 89.

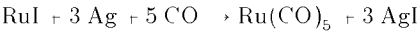
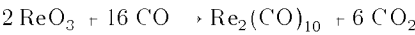
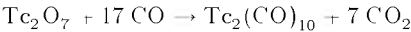
ⁱ Ref. 45.

Because transition metals even in a finely-divided state do not readily combine with CO, various metal salts have been used to synthesize metal carbonyls. Metal salts almost always contain the metal in a higher oxidation state than the resulting carbonyl complex. Therefore, most metal carbonyls result from the reduction of the metal in the starting material. Such a process has been referred to as reductive carbonylation. Although detailed mechanistic studies are lacking, the process probably proceeds through stepwise reduction of the metal with simultaneous coordination of CO (90).

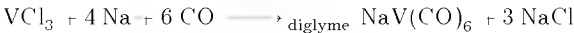
Syntheses from Dry Metals and Salts. Only metallic nickel and iron react directly with CO at moderate pressure and temperatures to form metal carbonyls. A report has claimed the synthesis of Co₂(CO)₈ in 99% yield from cobalt metal and CO at high temperatures and pressures (91,92). The CO has to be absolutely free of oxygen and carbon dioxide or the yield is drastically reduced. Two patents report the formation of carbonyls from molybdenum and tungsten metal (93,94). Ruthenium and osmium do not react with CO even under drastic conditions (95,96).

The dry method for synthesizing metal carbonyls from salts and oxides has proven very useful in a number of cases. The metal carbonyl is formed in the presence of a suitable reducing agent. In some cases CO itself is the reducing agent. Rhenium (97) and technetium (98,99) carbonyls are conveniently

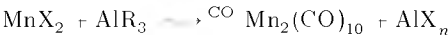
prepared from the oxides. Other suitable reducing agents, such as silver or copper, can be used in the dry state to effect carbonylation. Indeed the presence of Cu metal is deemed to be beneficial in the synthesis of $\text{Re}_2(\text{CO})_{10}$ by reaction of Re_2O_7 and CO for 16 h at 18.6 MPa (2700 psi) and 250°C (100).



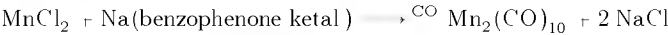
Syntheses in Solvent Systems. Very few examples of syntheses of metal carbonyls in aqueous solution are reported. An exception is the preparation of $\text{Co}_2(\text{CO})_8$ from CoSO_4 (66% yield) or CoCl_2 (56% yield) and CO at 9.6–11 MPa (95–110 atm) in aqueous ammonia at 120°C for 16–18 h (101). Triiron dodecacarbonyl is prepared almost exclusively in aqueous solution. Quantitative yields of $\text{Fe}_3(\text{CO})_{12}$ have been obtained by oxidizing alkaline solutions of carbonyl ferrates with manganese dioxide (102–104). Most metal carbonyls are synthesized in nonaqueous media. Reactive metals, such as sodium (85), magnesium (105), zinc (106), and aluminum (107,108), are usually used as reducing agents. Solvents that stabilize low oxidation states of metals and act as electron-transfer agents are commonly employed. These include diethyl ether, tetrahydrofuran, and 2-methoxyethyl ether (diglyme).



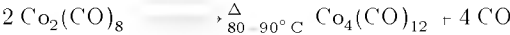
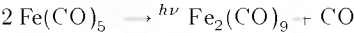
Reagents, such as trialkylaluminums (90) and sodium benzophenone (109), are quite useful as reducing agents. Alkylaluminums have been used to synthesize $\text{Cr}(\text{CO})$, $\text{Mo}(\text{CO})$, and $\text{W}(\text{CO})$ in high yields (90). In one case, hydrogen was used effectively as a reducing agent in petroleum ether solvent (110,111).



where X = Cl, I, HCO_2 , or CH_3CO_2 and R = CH_3 or C_2H_5



Condensation of Simple Metal Carbonyls. Some metal carbonyls of lower molecular weight lose CO on heating or uv irradiation leading to the formation of higher molecular weight species. In some cases this method is a useful preparative tool (112,113).

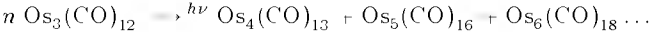


Carbonylation by CO Exchange. A few metal carbonyls can be prepared by exchange of CO molecules. The reaction of WCl_6 and $\text{Fe}(\text{CO})_5$ in the presence of hydrogen under pressure in diethyl ether results in yields of $\text{W}(\text{CO})$ as high as 85% (114). The same reaction can be used to synthesize $\text{Mo}(\text{CO})$ (115).

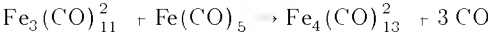
Synthesis of Heteronuclear and Polynuclear Metal Carbonyls. Heteronuclear metal carbonyls are usually synthesized either by metathesis (27) or addition (28,40).



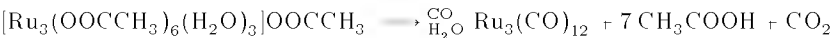
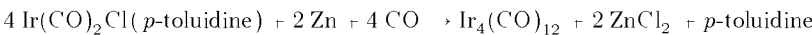
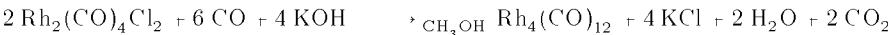
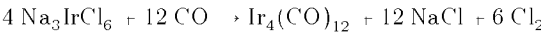
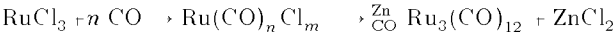
The main synthetic route to high nuclearity metal carbonyl clusters involves a condensation process: (1) a reaction induced by coordinatively unsaturated species; or (2) a reaction between coordinatively saturated species in different oxidation states. As an example of (1), $\text{Os}_3(\text{CO})_{12}$ can be condensed to form a series of higher coordinated species (89).



The interaction of species in different oxidation states can lead to higher coordinated molecules (54,116).



Low Pressure Syntheses. The majority of metal carbonyls are synthesized under high pressures of CO. Early preparations of carbonyls were made under superpressures of 1 GPa (ca 10,000 atm). Numerous reports have appeared in the literature concerning low pressure syntheses of metal carbonyls, but the reactions have been restricted primarily to the carbonyls of the transition metals of Groups 8–10 (VIII). A procedure for preparing $\text{Mn}_2(\text{CO})_{10}$, however, from commercially available methylcyclopentadienylmanganese tricarbonyl [12108-13-3] and atmospheric pressures of CO has been reported (117). The carbonyls of ruthenium (118,119), rhodium (120,121), and iridium (122,123) have been synthesized in good yields employing low pressure techniques. In all three cases, very low or even atmospheric pressures of CO effect carbonylation. Examples of successful low pressure syntheses are



An improved synthesis of Ru₃(CO)₁₂ by reaction of CO at 6.9 MPa (1,000 psi) and RuCl₃ ·xH₂O in anhydrous methanol at 125°C for 8 h has been reported (124). The systematics of the synthesis of transition-metal carbonyl cluster complexes has been reviewed (125).

Economic Aspects

Table 5 lists the metal carbonyls that are commercially available and the corresponding U.S. manufacturers or suppliers. Companies producing these compounds on a captive basis are not included.

Table 5. Commercial Availability of Metal Carbonyls

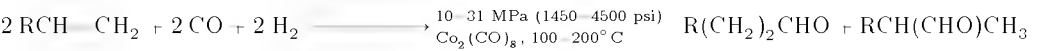
Metal carbonyl	Company ^a				Price, \$ g ^b
	Strem Chemicals	Pressure Chemical Co.	Aldrich Chemical Co.	Johnson Matthey (Aesar group)	
V(CO)	A		A		100
Cr(CO)	A	A	A	A	1
Mo(CO)	A	A	A	A	1
W(CO)	A	A	A	A	1
Mn ₂ (CO) ₁₀	A	A	A	A	3.50
Re ₂ (CO) ₁₀	A	A	A		11.50
Fe(CO) ₅ ^c	A	A	A		29 ^d
Fe ₂ (CO) ₉	A	A	A	A	1
Fe ₃ (CO) ₁₂	A	A	A	A	2
Ru ₃ (CO) ₁₂	A	A	A	A	16
Os ₃ (CO) ₁₂	A	A	A	A	90
Co ₂ (CO) ₈	A	A		A	0.50
Co ₄ (CO) ₁₂	A			A	3.50
Rh ₄ (CO) ₁₂	A				150
Rh (CO) ₁	A	A		A	150
Ir ₄ (CO) ₁₂	A				55
Ni(CO) ₄	A	A			161 ^d

^a Where A indicates the carbonyl is available in research-sized quantities of a few grams or kilograms.
^b Prices are approximate as of 1992.
^c GAF Corp. and BASF Corp. are bulk suppliers of Fe(CO)₅.
^d Price is in units of \$ kg.

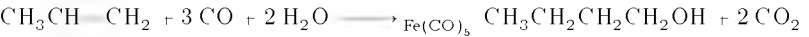
Use of Metal Carbonyls in Organic Synthesis

An extremely important field of chemistry concerned with stereospecific syntheses has developed around metal complexes that can give products having a high degree of optical purity (see PHARMACEUTICALS, OPTICALLY ACTIVE). The number of reactions involving transition metals and organic molecules is seemingly inexhaustible. Many of these reactions involve metal carbonyls, either as reagents or catalysts. Some of the catalytic reactions have important industrial applications.

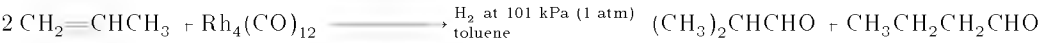
Carbonylation of Olefins. The carbonylation of olefins is a process of immense industrial importance. The process includes hydroformylation and hydrosilylation of an olefin. The hydroformylation reaction, or oxo process (qv), leads to the formation of aldehydes (qv) from olefins, carbon monoxide, hydrogen, and a transition-metal carbonyl. The hydrosilylation reaction involves addition of a silane to an olefin (126,127). One of the most important processes in the carbonylation of olefins uses Co₂(CO)₈ or its derivatives with phosphorus ligands as a catalyst. Propionaldehyde (128) and butyraldehyde (qv) (129) are synthesized industrially according to the following equation:



The oxo process is not limited to simple olefins. The terminal-to-branched ratio of products can be controlled by ligand addition (130). Butanol is produced from propylene and CO using a similar process (see BUTYL ALCOHOLS). The catalyst in this case is Fe(CO)₅ (131).



Tetrahodium dodecacarbonyl can effect carbonylation of an olefin at atmospheric pressure (132). The rate of hydroformylation of an olefin decreases with increasing alkyl substitution.



Straight-chain terminal olefins are more reactive than straight-chain internal olefins, which are more reactive than branched-chain olefins (133).

Carboxylation Reaction. The carboxylation reaction represents the conversion of acetylene and olefins into carboxylic acids (qv) or their derivatives. The industrially important Reppe process is used in the synthesis of β-unsaturated esters from acetylene. Nickel carbonyl is the catalyst of choice (134).

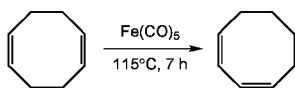


This process, to which the raw materials are supplied at low pressures, is continuous and gives good yields of acrylates (see ACRYLIC ACID AND DERIVATIVES). In the presence of catalytic amounts of Co₂(CO)₈, acetylene has been carboxylated in methanol yielding dimethyl succinate as the principal product (135).

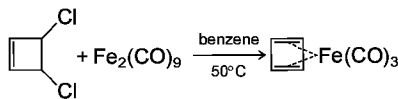
Allylic compounds can be carboxylated readily using Ni(CO)₄, either catalytically or stoichiometrically. In the presence of acetylene, the reaction of allylic compounds and CO, alcohols, and Ni(CO)₄ yields dienic carboxylic esters according to the following equation (136):



Olefin Isomerization. Some olefins can be isomerized in the presence of metal carbonyls. The carbonyl can act as a catalyst or a stoichiometric reagent in the reaction (137).

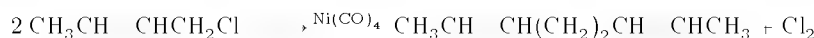


Stabilization of Unstable Intermediates. Transition metals can stabilize normally unstable or transient organic intermediates. Cyclobutadiene has never been isolated as a free molecule, but it has been isolated and fully characterized as an iron tricarbonyl complex (138):



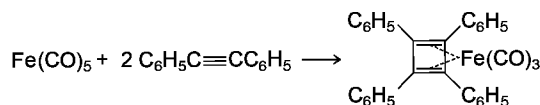
The complex exhibits remarkable stability, and the cyclobutadiene undergoes reactions without destruction of the ring (139). Cyclobutadieneiron tricarbonyl [12078-17-0] can be oxidized to generate cyclobutadiene *in situ* (140).

Coupling and Cyclization Reactions. An important process in organic chemistry is the coupling of alkyl halides to form longer-chain hydrocarbons. This process is classically referred to as the Wurtz reaction. Alkyl halides can be coupled using sodium metal in ethyl ether as the solvent, but the yields are normally low and the product impure. One of the most successful reagents for coupling alkyl halides is Ni(CO)_4 (141):



The process is versatile and a variety of long-chain hydrocarbons can be prepared.

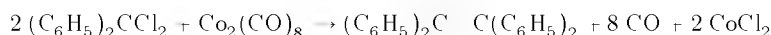
Reactions of acetylene and iron carbonyls can yield benzene derivatives, quinones, cyclopentadienes, and a variety of heterocyclic compounds. The cyclization reaction is useful for preparing substituted benzenes. The reaction of *tert*-butylacetylene in the presence of $\text{Co}_2(\text{CO})_8$ as the catalyst yields 1,2,4-tri-*tert*-butylbenzene (142). The reaction of Fe(CO)_5 and diphenylacetylene yields no less than seven different species. A cyclobutadiene derivative [31811-56-0] is the most important (143–145).



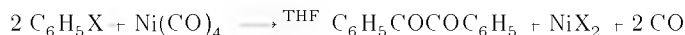
The reaction of $\text{Mn}_2(\text{CO})_{10}$ and acetylene yields π -dihydropentalenyl manganese (I) tricarbonyl [67375-48-8] (146):



Formation of Functional Groups. Metal carbonyls have been used in a number of cases to synthesize organic molecules containing particular functional groups (147–149). A synthesis of olefins from *gem*-dihalides has been reported (148):



Certain ketones (qv) can be synthesized conveniently from readily available aryl halides such as chloro- or bromobenzene (150,151).



Amines react with CO in the presence of metal carbonyls forming *N*-formyl derivatives or substituted ureas (152,153).

Homogeneous Hydrogenation Catalysis. Metal carbonyl complexes are generally soluble in organic solvents and can function as homogeneous catalysts (see CATALYSIS). Dicobalt octacarbonyl in the presence of hydrogen and CO reduces aldehydes to alcohols. In addition to aldehydes, other functional groups, such as imines, nitriles, nitroalkyls, and nitroaryls, can be reduced (154). Aqueous solutions of Fe(CO)_5 reduce nitrobenzenes to anilines (see AMINES BY REDUCTION), benzil to benzoin, and acetylenes to ethylene (155). Aqueous solutions of Fe(CO)_5 also convert olefins to alcohols at elevated temperatures and CO pressures (156). Fatty esters, such as methyl linoleate (157) and methyl linolenate (158), are reduced to varying degrees by Fe(CO)_5 in nonaqueous media at moderate hydrogen pressures.

The use of metal carbonyls in organic synthesis has been thoroughly reviewed (159–169).

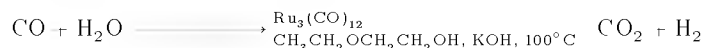
Industrial Uses

The main uses of metal carbonyls are in the areas of catalysis and organic synthesis. The Reppe synthesis and oxo process are both of enormous industrial importance.

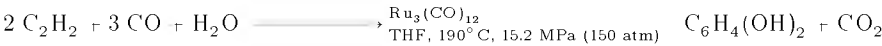
Easily decomposed, volatile metal carbonyls have been used in metal deposition reactions where heating forms the metal and carbon monoxide. Other products such as metal carbides and carbon may also form, depending on the conditions. The commercially important Mond process depends on the thermal decomposition of Ni(CO)_4 to form high purity nickel. In a typical vapor deposition process, a purified inert carrier gas is passed over a metal carbonyl containing the metal to be deposited. The carbonyl is volatilized, with or without heat, and carried over a heated substrate. The carbonyl is decomposed and the metal deposited on the substrate. A number of papers have appeared concerning vapor deposition techniques and uses (170–179).

Metal carbonyls have been used as antiknock compounds in unleaded gasoline (see GASOLINE AND OTHER MOTOR FUELS). The Ethyl Corp. marketed methylcyclopentadienylmanganese tricarbonyl (MMT); however, as in the case of tetraethyllead (180), its use is prohibited because of environmental concerns.

Alternative routes to synthetic fuels from less expensive and more abundant raw materials such as coal (qv) (see FUELS, SYNTHETIC) are being sought. An important method for converting coal into a more useful source of energy in certain applications is the water gas reaction (the high temperature reaction of carbon (coal) and water to give carbon monoxide and hydrogen). Water gas is an important industrial fuel and source of hydrogen (see HYDROGEN ENERGY). The hydrogen content of this gas may be increased by the water gas shift reaction, which is also catalyzed by metal carbonyls (181):



Removal of the CO_2 gives a mixture of CO and H_2 which is known as syngas. There is considerable interest directed toward converting syngas into simple organic compounds. The reaction of carbon monoxide and hydrogen to produce ethylene glycol in the presence of Rh(CO)_3 or other metal carbonyl derivatives as catalysts has been reported (182). Ethylene glycol, used as an antifreeze (qv), is produced from ethylene, which is itself a product of petroleum. The catalytic reaction described provides a means of synthesizing ethylene glycol from coal (see GLYCOLS). Metal carbonyls are also important sources of catalysts for the conversion of syngas into acetic acid (Monsanto process) and of methanol, CH_3OH , itself a syngas-derived material, into acetic anhydride $(\text{CH}_3\text{CO})_2\text{O}$ (Tennessee Eastman Halcon SD process) (see ACETIC ACID AND DERIVATIVES). The water gas shift reaction (183) may be involved in the carbonylation of acetylene with water as the hydrogen source to produce hydroquinone (see ACETYLENE DERIVED CHEMICALS).



An interesting development in the use of metal carbonyl catalysts is the production of hydrocarbons from carbon monoxide and hydrogen. The reaction of carbon monoxide and hydrogen in a molten solution of sodium chloride and aluminum chloride with Ir₄(CO)₁₂ as a catalyst yields a mixture of hydrocarbons. Ethane is the primary product (184).

Toxicology and Safety

Exposure to metal carbonyls can present a serious health threat. Nickel carbonyl is considered to be one of the most poisonous inorganic compounds. However, the toxicological information available on metal carbonyls is restricted to the more common, commercially important compounds such as Ni(CO)₄ and Fe(CO)₅. Other metal carbonyls are considered potentially dangerous, especially in the gaseous state, by analogy to nickel and iron carbonyls. Data concerning toxicological studies on a few common metal carbonyls are listed in Table 6 (185). Additional toxicity data are OSHA personal exposure limits (PEL): for Fe(CO)₅ this is 8 h at 0.1 ppm, whereas for the much more toxic Ni(CO)₄ it is 8 h at 0.001 ppm, with a toxic concentration TCL₀ low (of 7 mg m³) for human inhalation.

Table 6. Metal Carbonyls by Inhalation, 30 Minute LC₅₀ Values for Rats^a

Metal carbonyl	Carbonyl, mg m ³	Metal, mg m ³	Toxicity relative to Ni(CO) ₄	Reference
Ni(CO) ₄	240	85	1	186
HCo(CO) ₄	560	165	0.52	186
Fe(CO) ₅	910	260	0.33	187
	2190	625 (mice)	0.14	187
Co ₂ (CO) ₈	1400 ^b	480 ^b	0.17	188

^a Ref. 185.
^b A concentration that for 60 min resulted in no toxic signs.

The toxic symptoms from inhalation of nickel carbonyl are believed to be caused by both nickel metal and carbon monoxide. In many acute cases the symptoms are headache, dizziness, nausea, vomiting, fever, and difficulty in breathing. If exposure is continued, unconsciousness follows with subsequent damage to vital organs and death. Iron pentacarbonyl produces symptoms similar to nickel carbonyl but is considered less toxic than nickel carbonyl. When heated to about 60°C, nickel carbonyl explodes. For both iron and nickel carbonyl, suitable fire extinguishers are water, foam, carbon dioxide, or dry chemical. Large amounts of iron pentacarbonyl also have been reported to ignite spontaneously (189). Solutions of molybdenum carbonyl have been reported to be capable of spontaneous detonation (190). The toxicity of industrial chemicals including metal carbonyls may be found in references 191–194.

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CARBOXYLIC ACIDS

Survey,
Manufacture,
Economic aspects,
Fatty acids from tall oil,
Branched-chain acids,
Trialkylacetic acids,

SURVEY

Carboxylic acids from the smallest, formic, to the 22-carbon fatty acids, eg, erucic, are economically important; several million metric tons are produced annually. The shorter-chain aliphatic acids are colorless liquids. Each has a characteristic odor ranging from sharp and penetrating (formic and acetic acids), or vinegary (dilute acetic), to the odors of rancid butter (butyric acid), and goat fat (the 6–10-carbon acids). At room temperature, the cis-unsaturated acids through C₁₈ are liquids, and the saturated unbranched aliphatic acids from decanoic through the higher acids and trans-unsaturated acids are solids. The latter are higher melting because of their higher degree of linearity and greater degree of crystallinity eg, elaidic acid.

Although vegetable oils and animals fats were commonly used in ancient times, most higher acids were not known until the beginning of the nineteenth century. Then the nature of the naturally occurring 18-carbon fatty acids was established, and hundreds of long-chain fatty acids have been isolated from natural sources and characterized.

Both odd and even numbered alkanolic acids of molecular formula C_nH_{2n}O₂ occur naturally. Until chromatographic techniques provided means to identify minor components in natural mixtures, it was believed that only the even numbered higher acids, most often the C₁₈ acids, occurred naturally. Formic acid (qv), acetic acidacetic acid (qv), propionic, and butyric acids are manufactured in large quantities from petrochemical feedstocks. The higher fatty acids are derived from animal fats, vegetable oils, or fish oils. Some higher saturated fatty acids with significant industrial applications are caprylic, pelargonic, capric, lauric, myristic, palmitic, stearic, and behenic acids (Table 1).

Table 1. Physical Properties of the Straight-Chain Alkanolic Acids, C_nH_{2n}O₂

<i>n</i>	Systematic name (common name) ^a	CAS Registry Number	Mol wt	Mp, °C	Bp ^b , °C	Density ^c , g ⁰ ₄	Refractive index, <i>n</i> _D ^d	Δ <i>H</i> _f ^o at 25°C, kJ mol ^e	Specific heat, J g ^e	Heat of fusion, kJ mol ^e	Surface tension ^f , mN m (dyn cm)	Viscosity ^d , mPa·s (cP)	Δ <i>H</i> _R ²⁵ g ^g mol ^e
1	methanoic (formic) acid	[64-18-6]	46.03	8.4	100.5	1.220	1.3714						
2	ethanoic (acetic) acid	[64-19-7]	60.05	16.6	118.1	1.049	1.3718						
3	propanoic (propionic) acid	[79-09-04]	74.08	22	141.1	0.992	1.3874	511.2 (l)	2.34 (l)		20.7	1.099	1,536
4	butanoic (butyric) acid	[107-92-6]	88.11	7.9	163.5	0.959	1.39906	534.1 (l)	2.16 (l)		21.8	1.538	2,194
5	pentanoic (valeric) acid	[109-52-4]	102.13	34.5	187.0	0.942	1.4086	559.2 (l)				2.30	2,837.8
6	hexanoic ([caproic]) acid	[142-62-1]	116.16	3.4	205.8	0.929	1.4170	584.0 (l)	2.23 (l)	15.1	23.4	3.23	3,492.4
7	heptanoic ([enanthic]) acid	[111-14-8]	130.19	10.5	223.0	0.922	1.4230	609.1 (l)		15.0		4.33	4,146.9
8	octanoic ([caprylic]) acid	[124-07-2]	144.21	16.7	239.7	0.910	1.4280	635.2 (l)	2.62 (s)	21.4	23.7	5.74	4,799.9
9	nonanoic (pelargonic) acid	[112-05-0]	158.24	12.5	255.6	0.907	1.4322	658.5 (l)	2.91 (s)	20.3		8.08	5,456.1
10	decanoic ([capric]) acid	[334-48-5]	172.27	31.6	270.0	0.895 ³⁰	1.4169 ^f	685.2 (l)		28.0	25.0	4.30 ^h	6,108.7
11	undecanoic ([undecylic]) acid	[112-37-8]	186.30	29.3	284.0	0.9905 ²⁵	1.4202 ^f	736.7 (s)		25.1		7.30 ^h	6,762.3
12	dodecanoic (lauric) acid	[143-07-7]	200.32	44.2	298.9	0.883	1.4230 ^f	775.6 (s)	1.80 (s)	36.6	26.6	7.30 ^h	7,413.7
13	tridecanoic ([tridecylic]) acid	[638-53-9]	214.35	41.5	312.4	0.8458 ⁸	1.4252 ^f						
14	tetradecanoic (myristic) acid	[544-63-8]	228.38	53.9	326.2	0.858 ⁰	1.4273 ^f	835.9 (s)	1.60 (s)	44.8	27.4	5.83 ^f	8,721.4
15	pentadecanoic ([pentadecylic]) acid	[1002-84-2]	242.40	52.3	339.1	0.8423 ⁸	1.4292 ^f						
16	hexadecanoic (palmitic) acid	[57-10-3]	256.43	63.1	351.5	0.8534 ⁰	1.4309 ^f	892.9 (s)	1.80 (s)	54.4	28.2	7.80 ^f	10,030.6
17	heptadecanoic (margaric) acid	[506-12-7]	270.46	61.3	363.8	0.853 ⁰	1.4324 ^f						
18	octadecanoic (stearic) acid	[57-11-4]	284.48	69.6	376.1	0.847 ^f	1.4337 ^f	949.4 (s)	1.67 (s)	63.2	28.9	9.87 ^f	11,342.4
19	nonadecanoic ([nonadecylic]) acid	[646-30-0]	298.51	68.6	299 ¹⁰	0.8771 ²⁵	1.4512 ²⁵	1013.3 (s)		71.0			12,646.2
20	eicosanoic (arachidic) acid	[506-30-9]	312.54	75.3	203 ¹	0.8240 ¹	1.4250 ¹⁰	1063.7 (s)		78.7			13,976
21	docosanoic (behenic) acid	[112-85-6]	340.59	79.9	306 ¹	0.8221 ¹	1.4270 ¹⁰						
22	tetracosanoic (lignoceric) acid	[557-59-5]	368.65	84.2		0.8207 ¹	1.4287 ¹⁰						
23	hexacosanoic (cerotic) acid	[504-46-7]	396.	87.7		0.8198 ¹	1.4301 ¹⁰						

6		70	00	0
2	octacosanoic (montanic) acid	[506-48-9]	424.	
8			75	
3	triacontanoic (melissic) acid	[506-50-3]	452.	
0			81	
3	tritriacontanoic (psyllic) acid	[38232-03-	494.	
3		0]	89	
3	pentatriacontanoic (ceroplastic)	[38232-05-	522.	
5	acid	2]	94	

^a Brackets signify a trivial name no longer in use.
^b At 101.3 kPa 1 atm unless otherwise noted in kPa as a subscript.
^c At 20°C unless otherwise noted by a superscript number (°C).
^d At 20°C unless otherwise noted.
^e To convert J to cal, divide by 4.184.
^f At 70°C.
^g Heat of combustion (liquid).
^h At 50°C.
¹ To convert kPa to mm Hg, multiply by 7.5.

In the alkenoic series of molecular formula C_nH_{2n-2}O₂, acrylic, methacrylic, undecylenic, oleic, and erucic acids have important applications (Table 2). Acrylic and methacrylic acids have a petrochemical origin, and undecylenic, oleic, and erucic acids have natural origins (see ACRYLIC ACID AND DERIVATIVES; METHACRYLIC ACID AND DERIVATIVES).

Table 2. Physical Properties of the Straight-Chain Alkenoic Acids, C_nH_{2n-2}O₂

<i>n</i>	Systematic name (common name)	CAS Registry Number	Mol wt	Mp, °C	Bp, °C ^a	Density, ^b d ₄ ²⁰	Refractive index, ^b n _D ²⁰
3	propenoic (acrylic) acid	[79-10-7]	72.06	12.3	141.9	1.0621 ¹	1.4224
4	<i>trans</i> -2-butenic (crotonic) acid	[107-93-7]	86.09	72	189	1.018	1.4228 ^{79,7}
4	<i>cis</i> -2-butenic (isocrotonic) acid	[503-64-0]	86.09	14	171.9	1.0312 ¹⁵	1.4457
4	3-butenic (vinylacetic) acid	[625-38-7]	86.09	39	163	1.013 ¹⁵	1.4257 ¹⁵
5	2-pentenoic (β-ethylacrylic) acid	[626-98-2]	100.12				
5	3-pentenoic (β-pentenoic) acid	[5204-64-8]	100.12				
5	4-pentenoic (allylacetic) acid	[591-80-0]	100.12	22.5	188–189	0.9809	1.4281
6	2-hexenoic (isohydroascorbic) acid	[1191-04-4]	114.14				
6	3-hexenoic (hydrosorbic) acid	[4219-24-3]	114.14	12	208	0.9640 ²³	1.4935
7	<i>trans</i> -2-heptenoic acid	[10352-88-2]	128.17				
8	2-octenoic acid	[1470-50-4]	142.20				
9	2-nonenoic acid	[3760-11-0]	156.23				
10	<i>trans</i> -4-decenoic acid ^c ,	[57602-94-5]	170.25				
	<i>cis</i> -4-decenoic ^c	[505-90-8]					
10	9-decenoic (caproleic) acid	[14436-32-9]	170.25				
11	10-undecenoic (undecylenic) acid	[112-38-9]	184.28	24.5	275	0.9075 ²⁵	1.4464
12	<i>trans</i> -3-dodecenoic (linderic) acid	[4998-71-4]	198.31				
13	tridecenoic acid	[28555-21-7]	212.33				
14	<i>cis</i> -9-tetradecenoic (myristoleic) acid	[544-64-9]	226.36				
15	pentadecenoic acid	[26444-04-2]	240.39				
16	<i>cis</i> -9-hexadecenoic (<i>cis</i> -9-palmitoleic) acid	[373-49-9]	254.41				
16	<i>trans</i> -9-hexadecenoic (<i>trans</i> -9-palmitoleic) acid	[10030-73-6]	254.41				
17	9-heptadecenoic acid	[10136-52-4]	268.44				
18	<i>cis</i> -6-octadecenoic (petroselinic) acid	[593-39-5]	282.47	30		0.8681 ⁴⁰	1.4533 ⁴⁰
18	<i>trans</i> -6-octadecenoic (petroselaidic) acid	[593-40-8]	282.47	54			
18	<i>cis</i> -9-octadecenoic (oleic) acid	[112-80-1]	282.47	13.6	234 ^d	0.8905	1.4582 ³
18	<i>trans</i> -9-octadecenoic (elaidic) acid	[112-79-8]	282.47	43.7	234 ^d	0.8568 ⁷⁰	1.4405 ⁷⁰
18	<i>cis</i> -11-octadecenoic acid	[506-17-2]	282.47	14.5			
18	<i>trans</i> -11-octadecenoic (vaccenic) acid	[693-72-1]	282.47	44		0.8563 ⁷⁰	1.4406 ⁷⁰
20	<i>cis</i> -5-eicosenoic acid	[7050-07-9]	310.52				
20	<i>cis</i> -9-eicosenoic (godoleic) acid	[506-31-0]	310.52				
22	<i>cis</i> -11-docosenoic (cetoleic) acid	[506-36-5]	338.58				
22	<i>cis</i> -13-docosenoic (erucic) acid	[112-86-7]	338.58	34.7	281 ^e	0.85321 ⁷⁰	1.44438 ⁷⁰
22	<i>trans</i> -13-docosenoic (brassidic) acid	[506-33-2]	338.58	61.9	265 ^d	0.85002 ⁷⁰	1.44349 ⁷⁰
24	<i>cis</i> -15-tetracosenoic (selacholeic) acid	[506-37-6]	366.63				
26	<i>cis</i> -17-hexacosenoic (ximenic) acid	[544-84-3]	394.68				
30	<i>cis</i> -21-triacontenoic (lumequeic) acid	[67329-09-3]	450.79				

^a At 101.3 kPa 1 atm unless otherwise noted.
^b Superscript numbers indicate measurement at a temperature other than 20°C.
^c The common name for both *cis*- and *trans*-4-decenoic is obtusilic.
^d At 15 kPa 113 mm Hg.
^e At 30 kPa 225 mm Hg.

The polyunsaturated aliphatic monocarboxylic acids having industrial significance include sorbic, linoleic, linolenic, eleostearic, and various polyunsaturated fish acids (Table 3). Of these, only sorbic acid (qv) is made synthetically. The other acids, except those from tall oil, occur naturally as glycerides and are used mostly in this form.

Table 3. Some Polyunsaturated Fatty Acids

Total number of car-bon atoms	Systematic name (common name)	CAS Registry Number	Mol wt	Mp, °C	Bp at kPa ^a	Refrac-tive index, <i>n</i> _D ²⁰
<i>Dienoic acids</i> , C _n H _{2n-4} O ₂						
5	2,4-pentadienoic (β-vinylacrylic) acid	[626-99-3]	98.10			
6	2,4-hexadienoic ^b (sorbic) acid	[22500-92-1]	112.13	134.5		
10	<i>trans</i> -2,4-decadienoic acid	[3036-33-2]	168.24			
12	<i>trans</i> -2,4-dodecadienoic acid	[24738-48-5]	196.29			
18	<i>cis</i> -9, <i>cis</i> -12-octadecadienoic (linoleic) acid	[60-33-3]	280.45	5	202 at 1.4	1.4699
18	<i>trans</i> -9, <i>trans</i> -12-octadecadi-enoic (linolelaidic) acid	[506-21-8]	280.45	28–29		
18	5,6-octadecadienoic (laballic) acid	[5204-84-2]	280.45			
22	5,13-docosadienoic acid	[26764-24-9]	336.56			
<i>Trienoic acids</i> , C _n H _{2n-6} O ₂						
16	6,10,14-hexadecatrienoic (hiragonic) acid	[4444-12-6]	250.38			
18	<i>cis</i> -9, <i>cis</i> -12, <i>cis</i> -15-octadeca-trienoic (linolenic) acid	[463-40-1]	278.44	10 to 11.3	157 at 0.001	1.4800
18	<i>cis</i> -9, <i>trans</i> -11, <i>trans</i> -13-octa-decatrienoic (α-eleostearic) acid	[13296-76-9]	278.44	48–49	235 at 12	1.5112
18	<i>trans</i> -9, <i>trans</i> -11, <i>trans</i> -13-octa-decatrienoic (β-eleostearic) acid	[544-73-0]	278.44	71.5		1.5002
18	<i>cis</i> -9, <i>cis</i> -11, <i>trans</i> -13-octade-catrienic (punicic) acid	[544-72-9]	278.44			
18	<i>trans</i> -9, <i>trans</i> -12, <i>trans</i> -15-octadecatrienoic (linolenelaidic) acid	[28290-79-1]	278.44			
<i>Tetraenoic acids</i> , C _n H _{2n-8} O ₂						
18	4,8,12,15 octadecatetraenoic (morotcic) acid	[67329-10-6]	276.42			
18	<i>cis</i> -9, <i>trans</i> -11, <i>trans</i> -13, <i>cis</i> -15-octadecatetraenoic (α-parinaric) acid	[593-38-4]	276.42			
18	<i>trans</i> -9, <i>trans</i> -11, <i>trans</i> -13, <i>trans</i> -15-octadecate-traen oic (β-parinaric) acid	[18841-21-9]	276.42			
20	5,8,11,14-eicosatetraenoic (arachidonic) acid	[27400-91-5]	304.47			
22	4,8,12,15,19-docosapentae-noic (clupanodonic) acid	[2548-85-8]	330.51			
<i>Pentaenoic acids</i> , C _n H _{2n-10} O ₂						

^a To convert kPa to mm Hg, multiply by 7.5.
^b Δ*H*₂₉₈ 393.5 kJ mol⁻¹ (94.05 kcal mol⁻¹); flash point (OC) 127°C.

The shorter-chain alkynoic or acetylenic acids are common in laboratory organic syntheses, and several long-chain acids occur naturally (Table 4).

Table 4. The Acetylenic Fatty Acids

Total number of carbon atoms	Systematic name (common name)	CAS Registry Number	Mol wt
3	propynoic (propiolic, propargylic) acid	[471-25-0]	70.05
4	2-butynoic (tetrolic) acid	[590-93-2]	84.07
5	4-pentynoic acid	[6089-09-4]	98.10
6	5-hexynoic acid	[53293-00-8]	112.13
7	6-heptynoic acid	[30964-00-2]	126.16
8	7-octynoic acid	[10297-09-3]	140.18
9	8-nonynoic acid	[30964-01-3]	154.21
10	9-decynoic acid	[1642-49-5]	168.24
11	10-undecynoic (dehydro-10-undecylenic) acid	[2777-65-3]	182.26
18	6-octadecynoic (tariric) acid	[544-74-1]	280.45
18	9-octadecynoic (stearolic) acid	[506-24-1]	280.45
18	17-octadecene-9, 11-diynoic (isanic, erythrogenic) acid	[506-25-2]	274.40
18	<i>trans</i> -11-octadecene-9-ynoic (ximenynic) acid	[557-58-4]	278.44
22	13-docosynoic (behenolic) acid	[506-35-4]	336.56

Many substituted, ie, branched, fatty acids, particularly methacrylic, 2-ethylhexanoic, and ricinoleic acids, are commercially significant. Several substituted fatty acids exist naturally (Table 5). Fatty acids with a methyl group in the penultimate position are called iso acids, and those with a methyl group in the antepenultimate position are called anteiso acids (1) (see CARBOXYLIC ACIDS, BRANCHED CHAIN ACIDS). However, the term iso is often used in a broader sense to mean branched or mixtures of branched-chain industrial acids.

Table 5. Some Substituted Acids

Total	Systematic name (common name)	CAS Registry	Mol wt	Mp, °C	Bp, °C ^a	Density ^b	Refractive
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number of carbon atoms		Number				d_{4}^{20}	index ^b n_D^{20}
4	2-methylpropenoic (methacrylic) acid	[79-41-4]	86.09	16	163	1.0153	1.4314
4	2-methylpropanoic (isobutyric) acid	[79-31-2]	88.10	47	154.4	0.9504	1.3930
5	2-methyl- <i>cis</i> -2-butenic (angelic) acid	[565-63-9]	100.12	45	185	0.9539 ⁷	1.4434 ⁴⁷
5	2-methyl- <i>trans</i> -2-butenic (tiglic) acid	[80-59-1]	100.12	65.5	198.5	0.9641 ⁷	1.43297 ⁷
5	3-methyl-2-butenic (β,β-dimethyl acrylic) acid	[541-47-9]	100.12				
5	2-methylbutanoic acid	[116-53-0]	102.13				
5	3-methylbutanoic (isovaleric) acid	[503-74-2]	102.13	37.6	176	0.93319 ¹⁷	1.40178 ^{22,4}
5	2,2-dimethylpropanoic (pivalic) acid	[75-98-9]	102.13	35.5	163	0.905 ⁵⁰	
8	2-ethylhexanoic acid	[149-57-5]	144.21		220	0.9031 ²⁵	1.4255 ²⁸
14	3,11-dihydroxytetradecanoic (ipurolic) acid	[36138-54-2]	260.37				
16	2,15,16-trihydroxyhexadecanoic (ustilic) acid	[557-44-8]	304.43				
16	9,10,16-trihydroxyhexadecanoic (aleuritic) acid	[533-87-9]	304.43				
16	16-hydroxy-7-hexadecenoic (ambrettolic) acid	[506-14-9]	270.41				
18	12-hydroxy- <i>cis</i> -9-octadecenoic (ricinoleic) acid	[141-22-0]	298.47	5.0,7.7,16.0	226 ^c	0.9496 ¹⁵	1.4145 ¹⁵
18	12-hydroxy- <i>trans</i> -9-octadecenoic (ricinelaidic) acid	[540-12-5]	298.47	52–53	240 ^c		
18	4-oxo-9,11,13-octadecatrienoic (licanic) acid	[17699-20-6]	292.42				
18	9,10-dihydroxyoctadecanoic acid	[120-87-6]	316.48	90			
18	12-hydroxyoctadecanoic acid	[106-14-9]	300.48	79			
18	12-oxooctadecanoic acid	[925-44-0]	298.47	81.5			
18	18-hydroxy-9,11,13-octadecatrienoic (kamlolenic) acid	[4444-93-3]	294.43	77–78			
18	12,13-epoxy- <i>cis</i> -9-octadecenoic (vemolic) acid	[31263-20-4]	296.45				
18	8-hydroxy- <i>trans</i> -11-octadecene-9-ynoic (ximenynolic) acid		294.43				
18	8-hydroxy-17-octadecene-9,11-diynoic (isanolic) acid	[64144-78-1]	290.40				
20	14-hydroxy- <i>cis</i> -11-eicosenoic (lesquerolic) acid	[4103-20-2]	326.52				

^a At 101.3 kPa = 1 atm unless otherwise noted
^b Superscript numbers indicate measurement at a temperature other than 20°C.
^c At 1.3 kPa = 9.75 mm Hg.

Some naturally occurring fatty acids have alicyclic substituents such as the cyclopentenyl-containing chaulmoogra acids (1), notable for their use in treating leprosy (see ANTIPARASITIC AGENTS, ANTIMYCOTICS), and the cyclopropenyl (2) or sterculic acids (Table 6).

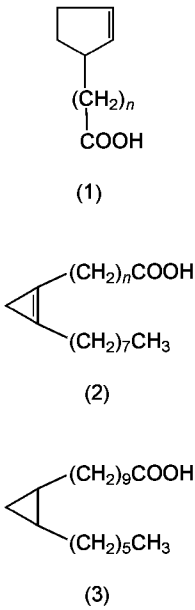


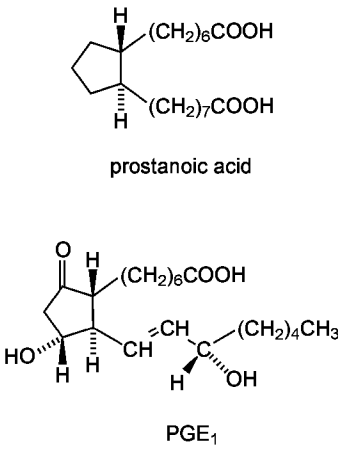
Table 6. Some Fatty Acids with Alicyclic Substituents

Total number of carbon atoms	Common name	CAS Registry Number	<i>n</i> in (1) or (2)	Mol wt
<i>Cyclopentenyl compounds^a</i>				
6	aleprolic	[2348-89-2]	0	112.13
10	aleprestic	[2348-90-5]	4	168.24
12	aleprylic	[24874-21-3]	6	196.29
14	alepric	[2519-24-6]	8	224.34
16	hydnocarpic	[459-67-6]	10	252.40
18	chaulmoogric	[502-30-7]	12	280.45
<i>Cyclopropenyl compounds^b</i>				
18	malvalic (halphenic)	[503-05-9]	6	280.45
19	sterculic	[738-87-4]	7	294.48
19	lactobacillic ^c	[503-06-0]		296.49

^a See structure (1).
^b See structure (2).

^c Saturated ring; see structure (3).

The prostaglandins (qv) constitute another class of fatty acids with alicyclic structures. These are of great biological importance and are formed by *in vivo* oxidation of 20-carbon polyunsaturated fatty acids, particularly arachidonic acid [27400-91-5]. Several prostaglandins, eg, PGE₁ [745-65-3], have different degrees of unsaturation and oxidation when compared to the parent compound, prostanoic acid [25151-18-9].



Aromatic carboxylic acids are produced annually in amounts of several million metric tons. Several aromatic acids occur naturally, eg, benzoic acid (qv), salicylic acid (qv), cinnamic acid (qv), and gallic acids, but those used in commerce are produced synthetically. These acids are generally crystalline solids with relatively high melting points, attributable to the rigid, planar, aromatic nucleus (see PHTHALIC ACIDS).

Nomenclature

Acyclic monocarboxylic acids are named substitutively by dropping the -e from the parent hydrocarbon name and adding -oic acid. Cyclic carboxylic acids are named substitutively by adding the suffix carboxylic acid to the name of the cyclic hydrocarbon. Positions of substituents, eg, amino-, chloro-, hydroxy-, methyl-, oxo-, in acyclic alkanolic acids are indicated by number locants, with the numbering starting from the carbon of the carboxyl group; in common names, Greek letters are used beginning at C-2 – the α-position. It is preferable to name substituted derivatives systematically and not on the basis of the common name for the parent compound, eg, 12-hydroxyoctadecanoic rather than 12-hydroxystearic acid. Acid halides of acyclic acids are named by dropping the ending -ic acid and adding the suffix -oyl or -yl to either the hydrocarbon name or the acid common name, eg, acetyl, hexanoyl, and stearyl chlorides from the respective names acetic acid, hexanoic, and stearic acid.

Esters are named by replacing the ending -ic acid with the suffix -ate. The alcohol portion of the ester is named by replacing the -ane ending of the parent hydrocarbon name with the suffix -yl. The alkyl radical name of an ester is separated from the carboxylate name, eg, methyl formate for HCOOCH₃. Amides are named by changing the ending -oic acid to -amide for either systematic or common names, eg, hexanamide and acetamide. Mono-, di-, and triunsaturated fatty acids are named with Arabic numeral locants for the unsaturated positions and with the suffix -enoic, -adienoic, and -atrienoic acid in place of the -ane ending of the saturated hydrocarbon name, eg, 10,12,14-octadecatrienoic acid.

Shorthand notations have been developed to avoid repetitive systematic names of unsaturated fatty acids. For example, linolenic or *cis*-9,*cis*-12,*cis*-15-octadecatrienoic acid can be represented by 18:3(9*c*,12*c*,15*c*). The Greek letter Δ has been used to indicate presence and position of double bonds, eg a Δ^{9,12,15} fatty acid, but it should never be used in a systematic name. An equally inappropriate but popular designation is derived by counting from the methyl terminus to the nearest double bond. For example, 9,12,15-octadecatrienoic, 9,12-octadecadienoic, and 9-octadecenoic acids are referred to as ω-3, ω-6, and ω-9, respectively.

Physical Properties

Melting points, boiling points, densities, and refractive indexes for carboxylic acids vary widely depending on molecular weight, structure, and the presence of unsaturation or other functional groups (Tables 1,2,3, and 5). In addition, some useful constants for alkanolic acids are listed in Table 1. Some constants for selected unsaturated and substituted acids are given in Table 7.

Table 7. Some Constants for Selected Unsaturated and Substituted Acids

Acid	Heat of formation, ^a kJ mol ^b	Flash point, °C	Heat of combustion, ^c kJ mol ^b
<i>Unsaturated acids</i>			
acrylic acid	384.3 (l)	49 ^d	
crotonic acid	431.6 (s)	88 ^d	
2-pentenoic acid	447.5 (s)		
3-pentenoic acid	435.3 (s)		
4-pentenoic acid	431.6 (l)		
undecenoic acid	572.2	146 ^d	6614
elaidic acid	786.1 (s)		11,154
oleic acid	802.9 (l)	189	11,228
brassicic acid	938.9		23,775
erucic acid	854.9 (s)		13,797
<i>Substituted acids</i>			
methacrylic acid	435.0 (l)		
isobutyric acid	534.1 (l)		2166
pivalic acid	565.1 (s)		2834

^a Δ*H*^o_f at 298 K.

^b To convert kJ to kcal, divide by 4.184.

^c Δ*H*^o_f (liquid).

^d OC – open cup.

Equations for the heat capacities in J /g for solid and liquid states of palmitic acid are, respectively (2)

$$C_p = 1.604 + 0.00544t \quad (-73 \text{ to } 40^\circ\text{C})$$
$$C_p = 1.936 + 0.00734t \quad (63 \text{ to } 92^\circ\text{C})$$

For stearic acid, the equations are (3)

$$C_p = 1.7886 + 0.00754t \quad (-120 \text{ to } 65^\circ\text{C})$$
$$C_p = 1.7861 + 0.00754t \quad (70 \text{ to } 78^\circ\text{C})$$

The viscosity of a mixture of fatty acids depends on the average chain length *n* and can be calculated from the equations (4):

$$\log \eta = -0.602802 + 0.134844n - 0.00259(n)^2 \quad (70^\circ\text{C})$$
$$\log \eta = -0.510490 + 0.101571n - 0.001628(n)^2 \quad (90^\circ\text{C})$$

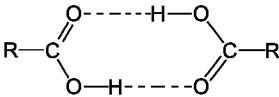
where *η* = viscosity in mPa·s(cP).

Heats of combustion for liquid alkanolic acids at 25°C are given by the equation (5):

$$\Delta H^{25} = 654.4n - 430.4 \text{ J /mol} \quad (n > 5)$$

Crystallographic properties of solid alkanolic acids significantly affect many of their other properties (6–8). For example, heat of crystallization, melting point, and solubility depend on whether the acid is even or odd numbered and vary alternately in a homologous series. Other physical properties such as boiling point, density (liquid), and refractive index depend on molecular rather than crystal structure. Thus these colligative properties change in a regular manner according to molecular weight.

The long-chain alkanolic acids and their derivatives are polymorphic with the unit cell containing dimers formed by hydrogen bonding between carboxyl groups.



In crystallizing fatty acids, solvent polarity does not influence crystal form as much as temperature and concentration (9). Infrared (9,10) and wide-line nmr spectra (11) as well as x-ray methods (12,13) can be used to detect the various crystalline forms.

Alkenolic acids also have polymorphic crystalline forms. For example, both oleic and elaidic acids are dimorphic with melting points of 13.6 and 16.3°C for oleic, and 43.7 and 44.8°C for elaidic acid (14).

The higher fatty acids undergo decarboxylation and other undesirable reactions when heated at their boiling points at atmospheric pressure. Hence they are distilled at reduced pressure (15,16). Methyl esters boil at lower temperatures than acids at the same pressure as the result of the absence of hydrogen bonding (17). A procedure for calculation of the vapor pressures of fatty acids at various temperatures has been described (18).

Formic, acetic, propionic, and butyric acids are miscible with water at room temperature. Solubility in water decreases rapidly for the higher alkanolic acids as the chain length increases (Table 8) (19). The solubility in water at pH 2–3 for unionized acids is given by the following relationship:

$$\log S = 0.6n + 2.32$$

where *S* = solubility in mol /L and *n* = number of carbon atoms (20).

Table 8. Solubilities of Alkanolic Acids in Water and Organic Solvents

Number of carbon atoms in RCOOH	Solubility at 20°C, g /100 g solvent				
	Water	Acetone	Benzene	Cyclohexane	<i>n</i> -Hexane
4	∞				
5	3.7				
6	0.968				
7	0.244				
8	0.068				
9	0.026	∞	∞	∞	∞
10	0.015	407	398	342	290
11	0.0093	706	663	525	
12	0.0055	60.5	93.6	68	47.7
13	0.0033	78.6	117	100	
14	0.0020	15.9	29.2	21.5	11.9
16	0.00072	5.38	7.3	6.5	3.1
18	0.00029	1.54	2.46	2.4	0.5

The hydrophilic nature of the carboxyl group balanced against the hydrophobic nature of the hydrocarbon chain allows long-chain fatty acids to form monomolecular films at aqueous liquid–gas, liquid–liquid, or liquid–solid interfaces (18).

The solubility of water in fatty acids, 0.92% for stearic acid at 68.7°C, is greater than the solubility of the acid in water, 0.0003% for stearic acid at 20°C, and this solubility tends to increase with increasing temperature (21). Solubilities of aliphatic acids in organic solvents demonstrate another example of the alternating effect of odd vs even numbered acids (Table 8).

An important chemical characteristic of unsaturated acids is the iodine value (IV), which indicates the average degree of unsaturation. It is equal to the number of grams of iodine absorbed under standard conditions by 100 g of the unsaturated acid.

Unsaturation in a fatty acid increases its solubility in organic solvents, and the differences in solubilities between saturated and unsaturated acids can be used to separate these acids (Table 9).

Table 9. Solubilities of Fatty Acids in Organic Solvents at Various Temperatures

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Fatty acid	Temperature, °C	Solubility, g /100 g solvent		
		Acetone	Toluene	<i>n</i> -Heptane
16:0	10	1.60	1.41	0.30
	0	0.66	0.36	0.08
	10	0.27	0.086	0.02
	20	0.10	0.018	0.005
18:0	10	0.54	0.390	0.080
	0	0.11	0.080	0.018
	10	0.023	0.015	0.004
	20	0.005	0.003	
18:1 (9 <i>c</i>)	20	5.2		2.25
	30	1.68	3.12	0.66
	40	0.53	0.96	0.19
	50	0.17	0.28	0.05
18:1 (9 <i>t</i>)	10		0.86	0.19
	−20	0.26	0.20	0.06
	−30	0.092	0.056	0.019
18:2 (9 <i>c</i> ,12 <i>c</i>)	50	4.10		0.98
	60	1.20		0.20
	70	0.35		0.042

Formic acid is the most acidic straight-chain alkanolic acid. Solubility in water of alkanolic acids containing more than nine carbon atoms is too low to permit accurate measurement of dissociation (Table 10). The acidity of 2-chloroalkanoic acids is much greater than that of formic acid, and trichloroacetic acid is comparable to the mineral acids in acid strength.

Table 10. Dissociation Constant *K_a* for Straight-Chain and Chlorinated Alkanoic Acids at 25°C

Acid	Unsubstituted	Cl at C-2
formic	2.1 × 10 ^{−4}	
acetic	1.81 × 10 ^{−5}	1.4 × 10 ^{−3}
propionic	1.32 × 10 ^{−5}	1.6 × 10 ^{−3}
butyric	1.50 × 10 ^{−5}	1.4 × 10 ^{−3}
pentanoic	1.56 × 10 ^{−5}	
hexanoic	1.40 × 10 ^{−5}	

Chemical Properties

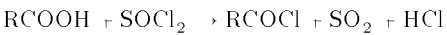
The alkanolic acids, with the exception of formic acid, undergo typical reactions of the carboxyl group. Formic acid has reducing properties and does not form an acid chloride or an anhydride. The hydrocarbon chain of alkanolic acids undergoes the usual reactions of hydrocarbons except that the carboxyl group exerts considerable influence on the site and ease of reaction. The alkenoic acids in which the double bond is not conjugated with the carboxyl group show typical reactions of internal olefins. All three types of reactions are industrially important.

Reactions of the carboxyl group include salt and acid chloride formation, esterification, pyrolysis, reduction, and amide, nitrile, and amine formation. *Salt formation* occurs when the carboxylic acid reacts with an alkaline substance (22)



where M = Li, Na, K, NH₄, R₃HN etc. The alkaline substance can also be an oxide, hydroxide, or carbonate of a metal of higher valence such as Ca, Mg, Zn, or Al. The saponification of fats and oils with caustic soda or potash gives water-soluble soaps. Water-insoluble, metallic soaps are prepared by fusion, precipitation, or direct solution of metal (see DRIERS AND METALLIC SOAPS). Fusion gives fine, dense, but slightly off-color metallic soaps useful as driers. The precipitation method forms fluffy, finely divided soaps of excellent color. Because of favorable economics, the former is becoming the method of choice for producing metal stearates. Lithium 12-hydroxyoctadecanoate [2918-92-5] is an important constituent of many greases.

Acid chlorides are prepared with reagents such as PCl₃, SOCl₂, (COCl)₂, and COCl₂ (23); preparation with thionyl chloride follows the reaction:

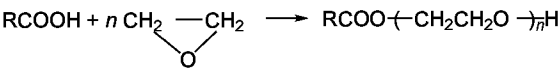


Fatty acid chlorides are very reactive and can be used instead of conventional methods to facilitate production of amides and esters. Imidazoles are effective recyclable catalysts for the reaction with phosgene (qv) (24).

Esterification is one of the most important reactions of fatty acids (25). Several types of esters are produced including those resulting from reaction with monohydric alcohols, polyhydric alcohols, ethylene or propylene oxide, and acetylene or vinyl acetate. The principal monohydric alcohols used are methyl, ethyl, propyl, isopropyl, butyl, and isobutyl alcohols (26) (see ESTERIFICATION; ESTERS, ORGANIC).

Sulfuric acid or hydrogen chloride may be used to catalyze esterification, and weight ratios of alcohol to fatty acid as high as 2 to 4:1, corresponding to molar ratios of 10 to 20:1, may be used to drive the equilibrium reaction to completion. Stoichiometric quantities of acid and alcohol can be used with hexyl and higher alcohols when the water of reaction is removed by azeotropic distillation with toluene or xylene. With long-chain fatty alcohols, water may be removed by azeotropic distillation, sparging with an inert gas, or subjecting the reaction to reduced pressure. Esters are also prepared by alcoholyses of animal fats or vegetable oils in the presence of alkaline or acidic catalysts (27,28). Esters of monohydric alcohols are used for plasticizers, as lubricants, and in cosmetics.

Esterification with polyhydric alcohols such as ethylene-, propylene-, diethylene-, and polyethylene glycols, glycerol, pentaerythritol, and certain carbohydrates is a more complex reaction because of immiscibility problems (see ALCOHOLS, POLYHYDRIC). A good reaction requires temperatures of 230–235°C and vigorous agitation in contrast to the milder conditions used for the simple alcohols. Temperatures higher than 235°C cause polyols to condense to ethers and to decompose. Nearly stoichiometric quantities of glycol and fatty acid are needed to make either monoesters or diesters. Product water is removed by reduced pressure, azeotropic distillation, or sparging. Monoesters are usually formed by reaction of ethylene or propylene oxide with the fatty acid:



The product is a mixture of various polyoxyethylene chain lengths (29–31). Glycol diesters are used as vinyl plasticizers; the monoesters as surface-active agents and viscosity modifiers for alkyd resins (qv).

Glycerol esterifications are still more complex (32–35). Even with excess glycerol (qv), a mixture of mono-, di-, and triglycerides is formed because of the limited solubility of glycerol in the reaction product. Nearly complete reaction of glycerol can occur at reduced pressure or in inert atmosphere and with 5–20° excess acid. Compositions of the reaction mixture can be calculated on a statistical basis assuming equivalence of the three hydroxyl groups and no isomer formation (33). Glycerides are important as surface-active agents; triolein [122-32-7] is used to some extent as a plasticizer (see SURFACTANTS; PLASTICIZERS).

Pentaerythritol with its four primary hydroxyl groups is used for the preparation of tetraesters and presents little difficulty except for its high melting point of 263°C, when pure. Pentaerythritol tetraesters are used in aircraft lubes, synthetic drying oils, and alkyds. Esters derived from trimethylolalkanes and dipentaerythritol are also used in alkyd resins (qv). Esterification may take place *in situ* during preparation of the alkyd.

Sorbitol is the most important higher polyol used in direct esterification of fatty acids. Esters of sorbitans and sorbitans modified with ethylene oxide are extensively used as surface-active agents. Interesterification of fatty acid methyl esters with sucrose yields biodegradable detergents, and with starch yields thermoplastic polymers (36).

Vinyl esters are prepared by the reaction of a fatty acid with either acetylene in direct condensation or vinyl acetate by acidolysis.

Reduction of fatty acids to alcohols is done by catalytic hydrogenation over a copper chromite catalyst at high temperatures of 325°C and pressures of 24 MPa (3500 psig) (37):



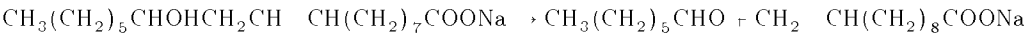
The yield of fatty alcohol is ca 90° . Fatty alcohols may also be prepared by high pressure catalytic hydrogenolysis of either a glyceride or a methyl ester. A copper chromite catalyst is used at 270–300°C and 34.6 MPa (5000 psig) of hydrogen pressure. If a glyceride is used, the yield of glycerol is relatively low because of hydrogenolysis to propylene glycol and isopropyl alcohol. The saturated fatty alcohols thus produced are used primarily in the production of detergents.

Reduction of glycerides or other esters with sodium and a secondary alcohol such as cyclohexanol or 4-methyl-2-pentanol was at one time a second commercial method for producing fatty alcohols. Though more costly than hydrogenolysis, this method gives high yields of glycerol and unsaturated fatty alcohols if the original fatty ester is unsaturated.

Selective hydrogenation of the carboxyl or ester group in preference to the olefinic unsaturation also produces unsaturated alcohols. Copper–cadmium and zinc–chromium oxides seem to provide most selectivity (38–42). Copper chromite catalysts are not selective. Reduction of red oil-grade oleic acid has been accomplished in 60–70° yield and with high selectivity with Cr–Zn–Cd, Cr–Zn–Cd–Al, or Zn–Cd–Al oxides (43). The reduction may be a homogeneously catalyzed reaction as the result of the formation of copper or cadmium soaps (44).

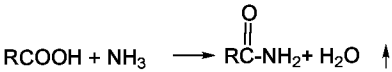
Pyrolysis of either saturated or unsaturated fatty acids leads to mixtures of hydrocarbons, olefins, and cyclic compounds (45). Pyrolysis of fatty acid salts or vegetable oils has been used to make hydrocarbon fractions suitable as petroleum substitutes. Various products are obtained by pyrolysis of fatty acid salts depending on the metal salt or catalyst used. Calcium salts generally form symmetrical ketones, aldehydes are formed in the presence of calcium formate, and hydrocarbons are formed in the presence of excess calcium hydroxide. Magnesium and lead salts produce ketones in improved yield over the calcium salts. Zinc oxide promotes hydrocarbon rather than ketone formation. Vapor-phase pyrolysis of fatty acids or esters over thorium or cesium oxides produces ketones in high yields. Homogeneous decarbonylation of fatty acid chlorides with PdCl₂ catalyst occurs readily at 185–200°C to make olefins in high yield (46).

Pyrolysis is used to produce undecenoic acid from ricinoleic acid:



Undecenoic acid is the starting point for making 11-aminoundecanoic acid [2432-99-7] and nylon-11 (see CASTOR OIL; POLYAMIDES).

Reactions of ammonia and amines with carboxylic acids result in the formation of a variety of products (47,48). Ammonium salts, RCOONH₄, are prepared with or without solvent, by reaction with anhydrous ammonia. Ammonium salts readily decompose to acid ammonium salts, RCOONH₄·RCOOH, particularly at temperatures higher than 50°C. Amides are formed at 150–200°C by reaction of the acid with ammonia at reduced pressures:

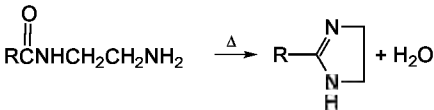


Amides are also formed by the reaction of an acid chloride with ammonia or an amine:



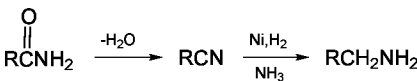
Ammonolysis or aminolysis of an ester can be used to make the respective amide or *N*-substituted amide.

Ammonium acetate and sodium methoxide are effective catalysts for the ammonolysis of soybean oil (49). Polyfunctional amines and amino alcohols such as ethylenediamine, ethanolamine, and diethanolamine react to give useful intermediates. Ethylenediamine can form either a monoamide or a diamide depending on the mole ratio of reactants. With an equimolar ratio of reactants and a temperature of >250°C, a cyclization reaction occurs to give imidazolines with ethylenediamine (48):



Ethanolamine produces oxazolines.

Fatty amines are made by dehydration of amides to nitriles at 280–330°C, followed by hydrogenation of the nitrile over nickel or cobalt catalysts:



The presence of ammonia during hydrogenation suppresses formation of secondary amines and inhibits hydrogenation of double bonds in unsaturated nitriles. Fatty amines are used as corrosion inhibitors, flotation agents, quaternary salts for sanitizing agents and textile fabric softeners, and surface-active agents.

Acyl aminimides have proved useful as surface-active and antimicrobial agents and as an intermediate for isocyanate preparation (50).

Reactions of the hydrocarbon chain in alkanolic acids include α-sulfonation and halogenation (51–54). The α-sulfonated fatty ester salts have excellent lime-dispersing properties and are valuable surface-active agents.

Reactions of the double bonds include isomerization and conjugation, cyclization, various addition reactions including hydrogenation, pyrolytic and

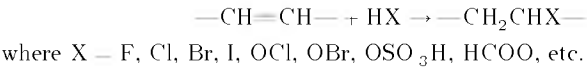
oxidative cleavage, metathesis, and various polymerization reactions (51,55).

Geometrical isomerization of cis- to trans-alkenoic acids occurs by photosensitization (56) or with heat treatment in the presence of catalysts such as SO₂, I₂, or HNO₂.

Positional isomerization occurs most often during partial hydrogenation of unsaturated fatty acids; it also occurs in strongly basic or acidic solution and by catalysis with metal hydrides or organometallic carbonyl complexes. Concentrated sulfuric or 70% perchloric acid treatment of oleic acid at 85°C produces γ-stearolactone from a series of double-bond isomerizations, hydration, and dehydration steps (57).

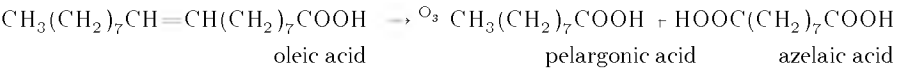
Conjugation as well as geometric and positional isomerization occur when an alkadienoic acid such as linoleic acid is treated with a strong base at an elevated temperature. Cyclic fatty acids result from isomerization of linolenic acid in strong base at about 250°C (58). Conjugated fatty acids undergo the Diels-Alder reaction with many dienophiles including ethylene, propylene, acrylic acid, and maleic anhydride.

Addition to the double bond occurs readily with hydrogen halides, hypohalous, sulfuric, or formic acids (53)

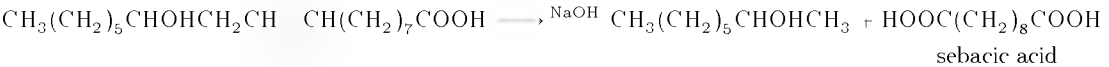


Addition of a weaker acid such as acetic acid takes place if the reaction is catalyzed by a sulfonic acid ion-exchange resin (59). Addition of halogens, mixed halogens, eg, the Wijs reagent ICl, or halogenlike compounds, eg, NOCl, and thiocyanogen, SCN₂, occurs easily and is the basis of several analytical methods for determining total unsaturation (60,61). Addition of hydrogen occurs only in the presence of an active catalyst such as nickel at moderately elevated temperatures and pressures (62). Other reagents that add to the double bond include carbon monoxide and hydrogen, eg, the oxo reaction (63,64); carbon monoxide and water, eg, hydrocarboxylation (64); various carbon free-radical compounds (65); dialkyl-phosphonates (66); formaldehyde (67); alcohols (68); rhodium-catalyzed olefin addition (69); and mercuric acetate (70). Dihydroxylation of a double bond may be brought about by peroxy acids or treatment with alkaline permanganate (71). Addition of oxygen is carried out with peroxy acids in the presence of strong acid catalysts to make epoxidized compounds (72).

Cleavage of an alkenoic acid can be carried out with permanganate, a permanganate–periodate mixture, periodate or with nitric acid, dichromate, ozone, or, if the unsaturation is first converted to a dihydroxy compound, lead tetraacetate (71,73). Oxidative ozonolysis is a process for the manufacture of azelaic acid [123-99-9] and pelargonic acid (74).



Alkali fusion of oleic acid at about 350°C in the Varrentrapp reaction causes double-bond isomerization to a conjugated system with the carboxylate group followed by oxidative cleavage to form palmitic acid (75). In contrast, alkali fusion of ricinoleic acid is the commercial route to sebacic acid [111-20-6]:



Metathesis of oleic acid to produce a C₁₈ straight-chain dibasic acid can be carried out at 70°C with a WCl₃·Sn(CH₃)₄ catalyst or with rhenium heptoxide promoted by Sn(CH₃)₄ (55,77).

Polymerization takes a variety of forms including dimerization or trimerization to polybasic acids. The internal double bond in oleic acid and other unsaturated fatty acids can participate, but only to a limited extent, in copolymerization with ethylene (78). Conjugated linoleate esters form co-oligomers with styrene by cationic catalysis (79). The resulting dibasic acid or ester can be condensed with ethyleneamine oligomers to make reactive polyamides useful for producing frothed epoxy compositions and as a catalyst for cross-linking rigid urethane foams (80). Conjugated linoleate esters are readily copolymerized with styrene and acrylonitrile by free-radical catalysis (81). Methyl eleostearate, however, inhibits copolymerization with either styrene or acrylonitrile. Polymerization of unsaturated fatty acids in drying oils through autooxidative mechanisms is the basis for a significant use of these materials in the paint industry (82) (see DRYING OILS).

Safety Information

Carboxylic acid dust and vapors are generally described as being destructive to tissues of the mucous membrane, eyes, and skin. The small molecules such as formic, acetic, propionic, butyric, and acrylic acids tend to be the most aggressive (Table 11) (83). Formic, acetic, propionic, acrylic, and methacrylic acids have time weighted-average exposure limits of 20 ppm or lower. Acrylic acid showed an LD₅₀ of 33.5 mg/kg from oral administration to rats.

Table 11. Safety and Toxicity

Total number of carbon atoms	Systematic name (common name) ^a	Flash point, °C	RTECS number	ACGIH ^b TWA, ppm	Rat ^c LD ₅₀ , mg/kg	DOT/IMO ^d label
1	methanoic (formic)		LQ4900000	5	1,100	corrosive
2	ethanoic (acetic)		AF1225000	10	3,530	corrosive flammable
3	propanoic (propionic)	54	UE5950000	10	2,600	corrosive
4	butanoic (butyric)	66	ES5425000		2,000	corrosive
5	pentanoic (valeric)	96 ^e	YV6100000		600 ^f	corrosive
6	hexanoic ([caproic])	102 ^e	MO5250000		3,000	corrosive
7	heptanoic ([enanthic])		MJ1575000		7,000	corrosive
8	octanoic ([caprylic])	132 ^e	RH0175000		10,080	
9	nonanoic (pelargonic)		RA6650000		3,200	
10	decanoic ([capric])		HD9100000			
11	undecanoic ([undecylic])		YQ2275000		140 ^f	
12	dodecanoic (lauric)		OE9800000		12,000	
13	tridecanoic ([tridecylic])		YD3850000			
14	tetradecanoic (myristic)		QH4375000			
15	pentadecanoic ([pentadecylic])		RZ1925000			
16	hexadecanoic (palmitic)		RT4550000			
17	heptadecanoic (margaric)		MI3850000			
18	octadecanoic (stearic)	196	WI2800000		4,640	
3	propenoic (acrylic)		AS4375000	2	33.5	corrosive
5	4-pentenoic (allylacetic)		SB2800000		470	
4	2-methylpropenoic (methacrylic)		OZ2975000	20	1,600 ^f	corrosive
4	2-methylpropanoic (isobutyric)		NQ4375000	280		corrosive, flammable
5	3-methyl-2-butenic (β, β-dimethyl		GQ5425000		3,560	

	acrylic)		
5	3-methylbutanoic (isovaleric)	NY1400000	2,000
5	2,2-dimethyl-propanoic (pivalic)	TO7700000	900
8	2-ethylhexanoate	MO7700000	3,000
11	10-undecenoic (undecylenic)	YQ2975000	2,500
18	cis-9-octadecenoic (oleic)	RG2275000	74,000
3	propynoic (propiolic)	UD9300000	100

^a Bracket signify a trivial name no longer in use.

^b ACGIU, American Conference of Governmental Industrial Hygienists; TWA, time-weighted average (8-h day or 40-h week).

^c LD₅₀, lethal dose 50^o o kill (oral), Rat.

^d DOT, Department of Transportation; IMO, International Maritime Organization.

^e Open cup.

^f Mouse.

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MANUFACTURE

Carboxylic acids having 6–24 carbon atoms are commonly known as fatty acids. Shorter-chain acids, such as formic, acetic, and propionic acid, are not classified as fatty acids and are produced synthetically from petroleum sources (see ACETIC ACID; FORMIC ACID AND DERIVATIVES; OXO PROCESS). Fatty acids are produced primarily from natural fats and oils through a series of unit operations. Clay bleaching and acid washing are sometimes also included with the above operations in the manufacture of fatty acids for the removal of impurities prior to subsequent processing.

The composition of common fats and oils are found in Table 1. The most predominant feedstocks for the manufacture of fatty acids are tallow and grease, coconut oil, palm oil, palm kernel oil, soybean oil, rapeseed oil, and cottonseed oil. Another large source of fatty acids comes from the distillation of crude tall oil obtained as a by-product from the Kraft pulping process (see TALL OIL; CARBOXYLIC ACIDS, FATTY ACIDS FROM TALL OIL).

Table 1. Fatty Acid Composition (%) and Significant Properties of Important Fats and Oils

Name	Chain length	Doubles	Cotton oil	Coconut oil	Palm kernel oil	Corn oil	Palm oil	Castor oil	Rapeseed oil (low erucic)	Rapeseed oil (high erucic)	Soybean oil	Sunflower oil	Herrings oil	Sardine oil	Tallow	Tall oil
caproic acid	C ₆	0		0–1	^a											
caprylic acid	C ₈	0		5–10	3–6											
capric acid	C ₁₀	0		5–10	3–5											
lauric acid	C ₁₂	0		43–53	40–52	0–1							^a			
myristic acid	C ₁₄	0	0–2	15–21	14–18		0–2		^a	^a	^a	^a	5–10	4–6	1–6	
palmitic acid	C ₁₆	0	17–29	7–11	6–10	8–19	30–48	2–3	3–6	0–5	7–12	3–10	11–16	9–11	20–37	1–3
stearic acid	C ₁₈	0	1–4	2–4	1–4	0–4	3–6	2–3	0–3	0–3	2–6	1–10	0–3	1–3	6–40	0–1
arachidic acid	C ₂₀	0	0–1				0–1		0–2	0–2	0–3	0–1			^a	0–1
behenic acid	C ₂₂	0	^a						^a	0–2	^a	0–1				
palmitoleic acid	C ₁₇	0–2							^a	^a	^a	0–1	5–12	10–15	1–9	
oleic acid	C ₁₈	1	13–44	6–8	9–16	19–50	38–44	4–9	50–66	9–25	20–30	20–40	8–15	15–25	20–50	9–16
gadoleic acid	C ₂₀	1	^a						0–5	5–15	0–1	^a				
erucic acid	C ₂₂	1							0–5	30–60		^a				
ricinoleic acid	C ₁₈	1						80–87								
linoleic acid	C ₁₈	2	33–58	1–3	1–3	34–62	9–12	2–7	18–30	11–25	48–58	50–70	2–4	3–8	0–5	20–32
linolenic acid	C ₁₈	3				0–2			6–14	5–12	4–10	0–1	0–2	1–3	0–3	
unsaturated fatty acids	C ₂₀	2–6							^a	^a			20–30	15–30	^a	^a
unsaturated fatty acids	C ₂₂	2–6							^a	0–2			10–28	15–20		
rosin acids																23–37
Properties																
iodine value, g I ₂ /100 g			96–112	8–12	14–23	103–128	44–54	81–91	105–120	91–108	120–140	120–140	120–145	170–193	35–55	
saponification value, mg KOH/g			190–198	250–264	245–255	188–193	194–206	174–186	185–188	170–175	190–195	186–189	178–194	189–193	190–200	130–170

^a Trace.

Manufacture of Fatty Acids from Natural Fats and Oils

There are essentially four steps or unit operations in the manufacture of fatty acids from natural fats and oils: (1) batch alkaline hydrolysis or continuous high pressure hydrolysis; (2) separation of the fatty acids usually by a continuous solvent crystallization process or by the hydrophilization process; (3) hydrogenation, which converts unsaturated fatty acids to saturated fatty acids; and (4) distillation, which separates components by their boiling points or vapor pressures. A good review of the production of fatty acids has been given (1).

Hydrolysis. Saponification or hydrolysis involves converting the fat or oil (a triglyceride) to a fatty acid and glycerol. This can be done in a number of ways including Twitchell splitting, autoclave batch splitting, continuous high pressure splitting, and enzymatic splitting. The feed should be of quality commensurate with the quality of fatty acid desired. Also, the feedstock generally is given a pretreatment such as clay bleaching or acid washing

prior to splitting that allows hydrolysis to take place more efficiently and to give a higher quality product in some cases (2).

Twitchell splitting is an acid catalyzed hydrolysis that uses sulfuric acid as the catalyst along with surface-active agents such as petroleum sulfonates or sulfonated oleic and naphthenic acids (Twitchell reagent). The splitting is carried out in acid-resistant vessels using about 60% fat or oil, 40% water, 0.5% sulfuric acid, and 1% petroleum sulfonate. The advantages of Twitchell splitting are its simple process and equipment required compared with the other methods. The disadvantages are darker colored products that usually contain traces of sulfur-containing materials, disposal of the aqueous acid layers, inefficient use of heat, and long cycle times. Twitchell splitting is used on a relatively small scale (3,4).

Autoclave batch splitting is generally carried out at 1.03–3.45 MPa (150–500 psig). By using certain metal oxides, such as zinc oxide, as catalysts, lower pressures can be used. In a typical batch the amount of water is about 30–60% of the fat weight. Headspace air is removed with steam to minimize oxidation and the autoclave is heated to the desired temperature and pressure. After 6–10 h a split of about 92% is obtained at the lower pressure whereas at higher pressures splits as high as 95% have been realized. After the desired degree of split is obtained the lower aqueous glycerol layer is separated from the upper fatty acid layer. If metal catalysts have been used the fatty acids are treated with sulfuric acid to decompose the soaps, and finally, any residual mineral acid is removed from the fatty acids with a hot water wash (5).

Continuous high pressure splitting was developed by Colgate-Emery and by Procter & Gamble (6,7). Temperatures of 240–270°C are preferred, giving pressures of 4.8–5.2 MPa (700–750 psig). The splitting is carried out in a cylindrical-shaped tower, 18.3–24.4 m high and 0.51–1.22 m in diameter of 316 L stainless steel or 316 L cladding on carbon steel. Splitting coconut oil requires better corrosion resistance because of the shorter-chain fatty acids present. Corrosion-resistant linings such as Carpenter 20 Cb or Incoloy 825 can be utilized. The tower is operated with countercurrent flow, with water being introduced into the top part of the tower and fat at the bottom of the tower. The tower contains disengaging zones where fatty acids are collected at the top of the tower and aqueous glycerol (sweet water) at the bottom (Fig. 1). Heat is conserved by the use of heat exchangers that cool the existing fatty acid while heating the incoming water (steam); the exiting sweet water is cooled by the entering fat, which in turn is heated in the exchanger. Make-up heat is applied to the center of the tower (the hydrolysis section containing the continuous fat phase) using internal steam coils, electric heating, or direct superheated steam. The pressure in the tower is controlled by a backpressure valve in the fatty acid discharge line, whereas the fat–sweet water interface is controlled by the rate of sweet water discharged. About 98–98.5% split is usually obtained. The sweet water contains 10–15% glycerol and is purified in a series of steps involving removal of any dissolved salts, fat, and oil impurities, and then concentration by evaporation of water and/or distillation (8). In some continuous high pressure splitting units, approximately 0.05% of ZnO catalyst is used to speed the reaction rates and raise conversion to >99.0%.

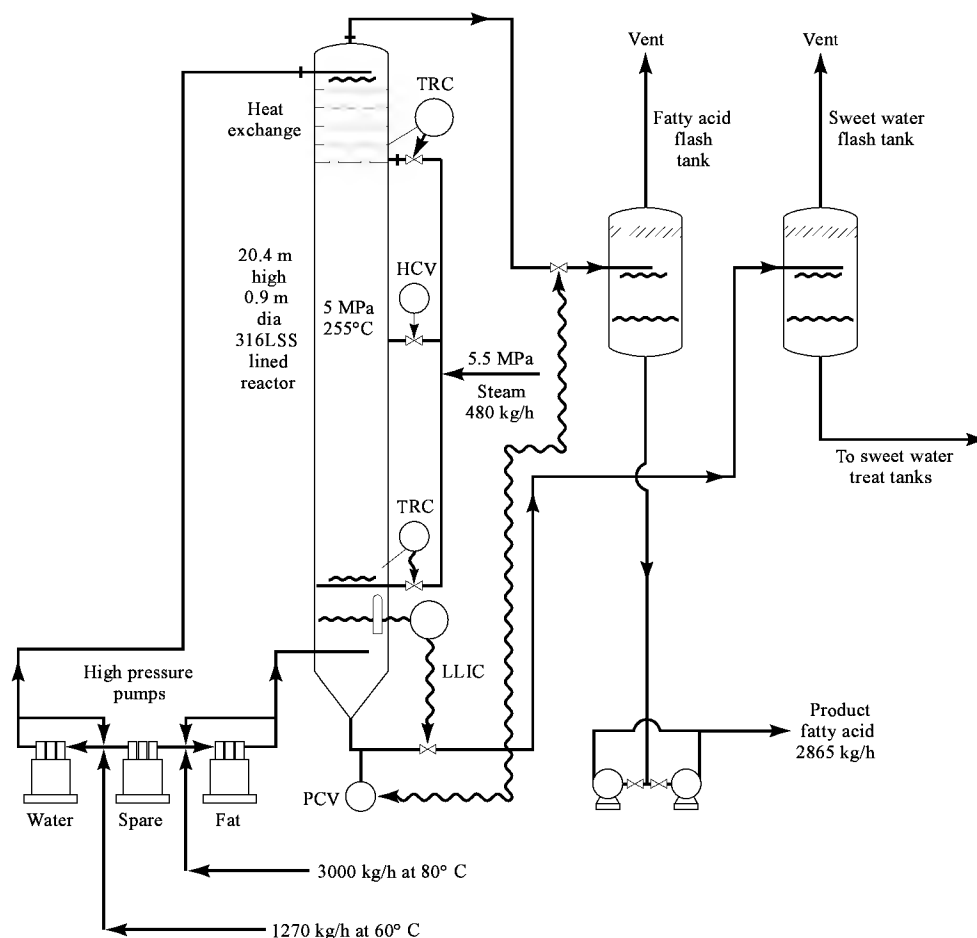


Fig. 1. Fat splitter. TRC, temperature recorder controller; LLIC, liquid level indicator controller; PCV, pressure control valve; and HCV, heat control valve. To convert MPa to psi, multiply by 145.

Enzymatic fat splitting was developed as a means to minimize energy costs and where a high order of specificity of splitting is desired. Enzymatic fat splitting is not currently carried out commercially in the United States but it is utilized in Japan where energy costs are high. Further details on enzymatic fat splitting are available (9).

Separation Techniques. Current methods for separating fatty acids are by solvent crystallization or by the hydrophilization process. Other methods that have been used in the past, or perhaps could be used in the future, are panning and pressing, solvent extraction, supercritical fluid extraction, the use of metal salts in assisting in separation, separations using urea complexes, and adsorption–desorption.

Panning and pressing is no longer used because of high labor costs, but it gave us the terms single-pressed, double-pressed, and triple-pressed stearic acid. These terms are widely used to denote the quality of stearic acid. These commercial "stearic" acids are actually mixtures of palmitic acid and stearic acid.

There are two commercial solvent crystallization processes. The Emersol Process, patented in 1942 by Emery Industries, uses methanol as solvent; and the Armour-Texaco Process, patented in 1948, uses acetone as solvent. The fatty acids to be separated are dissolved in the solvent and cooled, usually in a double-pipe chiller. Internal scrapers rotating at low rpm remove the crystals from the chilled surface. The slurry is then separated by means of a rotary vacuum filter. The filter cake is sprayed with cold solvent to remove free liquid acids, and the solvents are removed by flash evaporation and steam stripping and recovered for reuse (10).

When tallow fatty acids are the feed, stearic acid (actually 60–40 C16–C18) and oleic acids are the products. Solvent separation is also used to separate stearic acid from isostearic acid when hydrogenated monomer is the feed, and oleic acid from linoleic acid when using tall oil fatty acids as feed.

Several processes have been evaluated in attempts to lower the cost of the low temperature refrigeration required in the above solvent separation systems. The use of adiabatic cooling under vacuum to a temperature below the equilibrium temperature for crystallization has been described in which the resulting supercooled solution was transferred to a crystallization vessel where nucleation started and crystallization was reported to be complete within a few minutes. Spheroid-shaped crystals were obtained, which were more easily separated and washed than the usual crystals produced from other solvent processes (11). Two processes have been described in which crystallization occurs at a higher temperature. One uses methyl formate containing 5–10% water as solvent, where crystallization occurs about 15°C higher than when using methanol or acetone as solvent (12). The other process uses 2-nitropropane as solvent and gives a good separation of oleic acid from linoleic acid at 15°C instead of 30°C when using methanol or acetone as solvents (13).

To avoid the hazards and costs of using solvents, the Hydrophilization Process was developed by Henkel in Germany. The steps in the process include (1) cooling to obtain a slurry; (2) addition of aqueous solution of a wetting agent; (3) high speed agitation to form a dispersion of the solid fatty acid in the liquid; (4) addition of an electrolyte to stabilize the dispersion; and (5) separation of the solid fatty acid from the liquid fatty acid by means of a centrifuge. The quality of the products are generally not as good as when solvent separation is used (14–17).

Liquid–liquid extraction can be used to obtain high purity linoleic acid from safflower fatty acids or linoleic acid from linseed fatty acids using furfural and hexane as solvents (18). High purity linoleic acid has been obtained from sunflower fatty acids using a dimethylformamide and hexane solvent system (19).

Supercritical fluid extraction (SFE) has been investigated on oleochemical separations. This method uses a gas in the supercritical state, which generally means working at pressures of 8.3–48.5 MPa (1200–7000 psi), and at relatively low temperatures. Initial costs for commercial equipment can be quite high and will probably limit the use of SFE to higher priced specialty products (20). Methyl esters of Menhaden oil have been separated using supercritical CO₂ into docosa-hexaenoic acid [6217-54-5] (DHA) and eicosapentaenoic acid [10417-94-4] (EPA). These omega-3 fatty acids have been found to be important dietary factors, beneficial in reducing the development of atherosclerotic lesions. Accordingly, there is great interest in obtaining the polyunsaturated fatty acids present in fish oils in a more concentrated form (21).

Adsorption processes have recently been described to separate fatty acids into high purity products. Lauric acid was separated from myristic acid using crystalline silica as the adsorbent and was desorbed using a ketone such as acetone or methyl ethyl ketone (22). Another system, using cross-linked polystyrene as the adsorbent, separated a mixture of palmitic and stearic acids (23). Separation of saturated fatty acid, such as palmitic stearic acid from an unsaturated fatty oleic acid, using a molecular sieve plus crystalline clay as the adsorbent, has been described (24). The desorbent was acetone. The separation of oleic acid from linoleic acid has been described using as an adsorbent either cross-linked polystyrene, or a molecular sieve–silicate as the adsorbent with a variety of desorbents listed (25). Separation of fatty acids from rosin acids can be accomplished using molecular sieves that have been modified with silicalite and a phosphorus-modified alumina. The preferred desorbents were methyl ethyl ketone–acetic acid or short-chain acids or esters with less than six carbon atoms (26). The separation of fatty acids from unsaponifiables has been carried out using a molecular sieve, comprising a crystalline silica with a silica to alumina ratio of at least 12, as the adsorbent. The desorbent was acetone (27).

Hydrogenation. In the manufacture of fatty acids hydrogenation is used to saturate the ethylenic linkage to produce a more saturated acid. Generally, the feedstocks for hydrogenation are (1) the solid fractions from crystallizations where the iodine value (IV) is 4–15 and the desired IV after hydrogenation may be as low as 0.5; (2) tallow fatty acids to give a rubber-grade stearic acid having an IV of about 5–12; (3) coconut, palm, and palm kernel fatty acids to give hydrogenated products, which are then fractionated to give saturated fatty acids of six- to sixteen-carbon atoms; (4) fish fatty acid, such as menhaden, and high erucic rapeseed fatty acids to give arachidic (C-20) and behenic (C-22) acids; and (5) castor oil fatty acids (ricinoleic) to give 12-hydroxystearic acid. These and other feedstocks can be partially hydrogenated to give products having iodine values of about 20–80 that have found use in specific areas of application. Monomer acids, by-products from the dimerization of unsaturated fatty acids (primarily tall oil fatty acids), are hydrogenated to give a mixture of primarily stearic and isostearic acid, which are then separated from solvent by crystallization (28).

Hydrogenations can be carried out in batch reactors, in continuous slurry reactors, or in fixed-bed reactors. The material of construction is usually 316 L stainless steel because of its better corrosion resistance to fatty acids. The hydrogenation reaction is exothermic and provisions must be made for the effective removal or control of the heat; a reduction of one IV per g of C₁₈ fatty acid releases 7.1 J (1.7 cal), which raises the temperature 1.58°C. This heat of hydrogenation is used to raise the temperature of the fatty acid to the desired reaction temperature and is maintained with cooling water to control the reaction.

The size of a typical batch reactor is 18–23 t. Some reactors have a hydrogen recycle system, whereas in others the hydrogen is internally recycled by the use of a hollow agitator shaft that allows hydrogen to be drawn from the head space to below the impeller blades where it mixes with the liquid fatty acids. This recycle of the hydrogen gives better contact with the liquid and effective mixing does not have to depend solely on agitation. It is also an advantage to vent some of the hydrogen periodically, which allows removal of inert material and possibly catalyst poisons (29).

Continuous slurry reactors are generally either of one of two designs. One type uses a reactor loop, generally known as a Buss loop design; the other is a co-current hydrogen fatty acid catalyst system mainly marketed by Lurgi. Continuous slurry reactors are more popular in Europe, Asia, and South America than in the United States.

Fixed-bed reactors have been described in detail and their advantages and disadvantages listed (29). It is reported that only one manufacturer uses fixed-bed hydrogenation for fatty acids (29).

Dry reduced nickel catalyst protected by fat is the most common catalyst for the hydrogenation of fatty acids. The composition of this type of catalyst is about 25% nickel, 25% inert carrier, and 50% solid fat. Manufacturers of this catalyst include Calsicat (Mallinckrodt), Harshaw (Engelhard), United Catalysts (Sbd Chemie), and Unichema. Other catalysts that still have some place in fatty acid hydrogenation are so-called wet reduced nickel catalysts (formate catalysts), Raney nickel catalysts, and precious metal catalysts, primarily palladium on carbon. The spent nickel catalysts are usually sent to a broker who sells them for recovery of nickel value. Spent palladium catalysts are usually returned to the catalyst supplier for credit of palladium value.

The most important reaction variables in the hydrogenation of fatty acids are temperature, pressure, agitation, catalyst loading, and catalyst addition. Temperature is normally in the range of 150 to 210°C. Below 150°C the nickel catalyst is not activated sufficiently; however, above 210°C some degradation may occur, which could inactivate the catalyst thus slowing the reaction rate. Pressures of industrial hydrogenations are about 2.08–3.47 MPa (300–500 psig). Pressures below 2.08 MPa require longer times to reach the same IV if the hydrogenation is carried out at 3.47 MPa. Pressure higher than 3.47 MPa has little or no effect on reaction rate. Increasing the agitation in the reactor increases the reaction rate. Determination of the optimum level of agitation is dependent on the configuration inside each specific reactor. Because the reaction is mass and diffusion limited, increasing the speed of the agitator increases the dispersion of catalyst in the fatty acid until it reaches a maximum that corresponds to a maximum reaction rate, assuming everything else is constant. Proper agitation also helps to keep the solid catalyst in suspension, to help maintain temperature control, and to bring the hydrogen in contact with the catalyst fatty acid. Increasing the catalyst loading increases the reaction rate. However, when extremely large amounts of catalysts are used it may cause a rapid decrease in hydrogen concentration in the fatty acid resulting in a dehydrogenation reaction. The optimum time of catalyst addition is near the reaction temperature and immediately thereafter hydrogen is introduced. Prolonged exposure of a nickel catalyst to hot fatty acids leads to catalyst deactivation (29).

The quality of the feedstock is important since it affects not only the product quality but the rate of hydrogenation. Some of the impurities that affect the rate are sulfur, phosphorus, halides, polyethylene, and moisture. Impurities are usually removed by clay treatment or by distillation (30).

Distillation. Most fatty acids are distilled to produce high quality products having excellent color and a low level of impurities. Distillation removes odor bodies and low boiling unsaponifiable material in a light ends or heads fraction, and higher boiling material such as polymerized material, triglycerides, color bodies, and heavy decomposition products are removed as a bottoms or pitch fraction. The middle fractions sometimes can be used as is, or they can be fractionated (separated) into relatively pure materials such as lauric, myristic, palmitic, and stearic acids.

Because fatty acids, and especially unsaturated fatty acids, have limited stability when subjected to high temperatures, most distillations are carried out in continuous distillation columns as opposed to batch-type distillations. Almost all distillations are carried out under vacuum and sometimes with the

injection of steam to further reduce the temperature at which the fatty acid will distill. Boiling points of various fatty acids at different pressures are shown in Table 2.

Table 2. Boiling Points of Fatty Acids,^a °C

Pressure, kPa ^b	Caproic acid	Caprylic acid	Capric acid	Lauric acid	Myristic acid	Palmitic acid	Stearic acid	Oleic acid	Linoleic acid
0.133 kPa	61.7	87.5	110.3	130.2	149.2	167.4	183.6	177.6	178.5
0.267 kPa	71.9	97.9	121.1	141.8	161.1	179.0	195.9	189.5	190.1
0.533 kPa	82.8	109.1	132.7	154.1	173.9	192.2	209.2	202.6	202.8
1.07 kPa	94.6	121.3	145.5	167.4	187.6	206.1	224.1	217.0	216.9
2.13 kPa	107.3	134.6	159.4	181.8	202.4	221.5	240.0	232.9	232.6
4.27 kPa	120.8	149.2	174.6	197.4	218.3	238.4	257.1	250.6	250.0
8.53 kPa	136.0	165.3	191.3	214.6	236.3	257.1	276.8	270.3	269.7
17.1 kPa	152.5	183.3	209.8	234.3	257.3	278.7	299.7	292.5	291.9
34.1 kPa	171.5	203.0	230.6	256.6	281.5	303.6	324.8	317.7	317.2
68.3 kPa	192.5	225.6	254.9	282.5	309.0	332.6	355.2	346.5	346.5
101.3 kPa	205.8	239.7	270.0	298.9	326.2	351.5	376.1	364.9	365.2

^a Ref. 31.

^b To convert kPa to mm Hg, multiply by 7.5

The crude fatty acid feed is usually preheated and degassed to remove air and water. If a vapor feed is desired it is then flashed in a vaporizer and fed to the distillation column as a vapor or vapor–liquid. A continuous distillation using one column will generally produce a satisfactory product if a suitable feedstock is used. If the feedstock contains large amounts of low boilers, color, and odor bodies, it is then preferable to use a two-column system. The low boilers and odor are removed as a heads fraction in the first column; the remaining material is removed at the bottom and then fed to a second column where a residue cut is taken off the bottom and the desired fatty acid fraction is removed as a side stream. It is possible to use a one-column system if the side stream is taken in the stripping section below the feed and taken as a vapor and condensed. Doing this will eliminate any high boilers in the side steam.

Most distillation columns in the past used sieve trays or bubble cap trays where the pressure drop could be substantial (1–2 mm tray) or about 30–50 mm in a column of 20–30 trays. Because of this pressure drop the distillation temperature must be higher and this higher temperature causes some decomposition of the fatty acids. A packing called structured packing has low pressure drop per theoretical plate thus making it ideal for use in the distillation of heat-sensitive fatty acids. It is available throughout the world as either Flexipac or Mellapac (31). Wiped-film evaporators can be used in the distillation of heat-sensitive material because the contact time with a hot surface is extremely short. They have also been used in depitching crude tall oil (31).

Fatty acids are corrosive at high temperatures and selection of materials of construction for distillation systems is critical. Stainless steels with various contents of molybdenum have proved satisfactory. For example, 316 L has 2% Mo and is satisfactory for service up to 260°C; 317 L has 3% Mo and can be used satisfactorily up to 285°C, whereas 904 L can be used up to 310°C (31).

Synthetic Routes to Fatty Acids from Petroleum

These synthetic processes have been reviewed in detail (32).

Catalytic Oxidation for Straight-Chain Paraffinic Hydrocarbons. Synthetic fatty acids (SFA) are produced by Eastern European countries, Russia, and China using a manganese-catalyzed oxidation of selected paraffinic streams. The technology is based on German developments that were in use during World War II. The production volume in 1984 was estimated to be about 5.5 × 10⁵ t yr. The oxidation is highly exothermic and is carried out at about 105–125°C, mostly in continuous equipment.

Oxidation of Straight-Chain 1-Olefins. Oxidation of α-olefins has been thoroughly studied using ozone, peracids, nitric acid, chromic acid, and others.

Carboxylation/Oxidation of Straight-Chain 1-Olefins. Selective carboxylation of α-olefins to predominately straight-chain aldehydes is realized through specific catalyst systems and by careful control of reaction conditions. The aldehyde produced is then air-oxidized to the acid using a Mn catalyst. Heptanoic acid [111-14-8] and pelargonic acid [112-05-0] are produced commercially in this manner.

Carboxylation of Straight-Chain 1-Olefins. Carboxylation is the selective addition of CO and water to an olefin to give either a straight-chain or branched-chain acid. The use of specific catalysts and reaction conditions has given a straight-chain branched-chain isomer ratio as high as 98:2. In spite of a one-step method to predominately straight-chain isomers of fatty acids, no commercialization using this route has yet occurred in the United States.

Oxidation of Straight-Chain Alcohols. Two methods have been developed. One uses an air oxidation catalyzed by a metal, eg, copper, platinum, etc, whereas the other is a caustic oxidation. Generally, however, fatty alcohols are priced higher on the world market than their corresponding fatty acids and, consequently, these conversions are uneconomical.

Branched-Chain Carboxylic Acids. Branched-chain acids such as 2-methylbutyric, 3-methylbutyric, isooctanoic, and isononanoic acids are produced by the oxo reaction, giving first the corresponding aldehyde, which is then oxidized to the acid. 2-Ethylhexanoic acid is produced by the aldol route from butyaldehyde in three steps: aldol condensation; hydrogenation of the carbon–carbon double bond; and oxidation of the branched-chain saturated aldehyde to 2-ethylhexanoic acid (see CARBOXYLIC ACIDS, BRANCHED CHAIN ACIDS).

Highly Branched Acids. These acids, called neoacids, are produced from highly branched olefins, carbon monoxide, and an acid catalyst such as sulfuric acid, hydrogen fluoride, or boron trifluoride. 2,2,2-Trimethylacetic acid (pivalic acid) is made from isobutylene and neodecanoic acid is produced from propylene trimer (see CARBOXYLIC ACIDS, TRIALKYLACETIC ACIDS).

Environmental Aspects

Environmental regulation in the oleochemical industry addresses pollution of air, surface, and groundwater, along with land pollution and solid waste disposal. This is administered by the Environmental Protection Agency (EPA) on the national level, an equivalent agency on the state level, and sometimes local agencies also deal with various aspects of pollution abatement.

In-plant controls are perhaps the best approach to eliminate waste generation and pollution problems, and many times good payback exists on recovery of products lost because of poor process controls. If the production department is responsible for the generation and in-plant control of wastes, this will help ensure that initial standards for water use and process loss are reasonable and that they are maintained (33).

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ECONOMIC ASPECTS

Aliphatic carboxylic acids produced on a reasonably significant commercial scale range from acetic acid (two carbons or C2) through stearic acid (C18). Lesser amounts of commercially available shorter chain-length acids, such as formic (C1), and longer chain-length acids, such as erucic (unsaturated C22) and behenic (saturated C22), are also produced. As a general rule, all of the even chain-length, nonisomeric acids from C6 to C22 are produced from naturally occurring fats and oils. A significant proportion of the lower chain-length (C1–C6) and longer isomeric chain-length (C7–C10) acids are made synthetically.

Nonoleo-Based Carboxylic Acids

Some of the more prominent carboxylic acids that are not fat- or oil-based include acetic, acrylic, and olefin-based propionic, butyric isobutyric, 2-ethylhexanoic, heptanoic, pelargonic, neopentanoic, and neodecanoic. Table 1 summarizes the production, pricing, and primary producers of these acids.

Table 1. 1988–1991 U.S. Statistics on Non-Fat and Oil-Based Acids^a.

Acid	Production, 10 ³ t	Price, \$ kg	Producers	Applications
acetic (C2)	1538	0.62–0.68	Borden, Eastman, Hoechst Celanese, Quantum, Sterling, Union Carbide	vinyl acetate; acetic anhydride; acetate esters; TPA DMT plastics
acrylic (C3)	490	1.45	BASF, Hoechst Celanese, Rohm & Haas, Union Carbide	acrylate esters (latex coatings, adhesives, polishes, etc)
propionic (C3)	54	0.73–0.82	Eastman, Hoechst Celanese, Union Carbide	grain and feed preservative; propionate salts; pesticides; cellulose acetate
butyric isobutyric (C4)	24		Eastman, Hoechst Celanese	cellulose acetate butyrate (plastic); pesticides (isobutyric)
2-ethylhexanoic (C8)	12	1.25	Eastman, Union Carbide	paint driers; heat stabilizers for PVC
benzoic (C7)	43	1.21–3.86	Kalama, Pfizer, Velsicol	benzoate plasticizers; benzoate salts (preservative)
heptanoic pelargonic (C7 C9)	20	1.40–1.80	Hoechst Celanese	polyol esters for synthetic lubricants; tetraethylene glycol diheptanoate plasticizer
neoacids (C5–C10)	18	1.30–2.15	Exxon	peroxy esters (polymerization initiators); pivaloyl chloride (polymerization, pharmaceuticals)

^a Ref. 1

With the exception of acetic, acrylic, and benzoic all other acids in Table 1 are primarily produced using oxo chemistry (see [OXO PROCESS](#)). Propionic acid is made by the liquid-phase oxidation of propionaldehyde, which in turn is made by application of the oxo synthesis to ethylene. Propionic acid can also be made by oxidation of propane or by hydrocarboxylation of ethylene with CO and H₂ in the presence of a rhodium (2) or iridium (3) catalyst.

Butyric acid is made by air-oxidation of butyraldehyde, which is obtained by application of the oxo synthesis to propylene. Isobutyric acid is made from isobutyraldehyde, a significant product in the synthesis of butyraldehyde (see [BUTYRALDEHYDES](#)). Butyraldehyde is also used to make 2-ethylhexanoic acid.

Rhodium catalyst is used to convert linear alpha-olefins to heptanoic and pelargonic acids (see [CARBOXYLIC ACIDS, MANUFACTURE](#)). These acids can also be made from the ozonolysis of oleic acid, as done by the Henkel Corp. Emery Group, or by steam cracking methyl ricinoleate, a by-product of the manufacture of nylon-11, an Atochem process in France (4). Neoacids are derived from isobutylene and nonene (4) (see [CARBOXYLIC ACIDS, TRIALKYLACETIC ACIDS](#)).

Acetic acid (qv) can be produced synthetically (methanol carbonylation, acetaldehyde oxidation, butane naphtha oxidation) or from natural sources (5). Oxygen is added to propylene to make acrolein, which is further oxidized to acrylic acid (see [ACRYLIC ACID AND DERIVATIVES](#)). An alternative method adds carbon monoxide and or water to acetylene (6). Benzoic acid (qv) is made by oxidizing toluene in the presence of a cobalt catalyst (7).

Oleo-Based Carboxylic Acids

Worldwide capacity for production of higher aliphatic carboxylic acids (predominantly C8–C18), commonly called fatty acids, is about 3.5 million metric tons, with an additional 400,000 metric tons because of start-up over the next 1–2 years, mostly in southeast Asia. Worldwide production of these higher (and linear) fatty acids in 1988 was estimated at 2.6 million metric tons, with annual growth estimated at 2–3% (8). U.S. production of these C8–C18 linear acids, including tall oil (9), was reported to be approximately 660,000 metric tons, a figure that would appear to be understated. The use of these fatty acids covers many consumer product and industrial applications and historically has correlated well with the GNP in the United States.

Typically, fatty acids make up between 87 and 90% of the fat or oil from which they are made; the remaining 10–13% is glycerol. The most often used raw materials are coconut or palm kernel oil (lauric oils) for C8, C10, C12, and C14 acids; tallow, lard, and palm stearine for C16 and C18 acids; and soybean, sunflower, canola, and tall oil for whole cut unsaturated (lower melting point) acids. Fully hardened soya, canola, or edible tallow are usually used when high C18 food-grade stearic acid is needed, whereas edible tallow and tall oil are the primary raw materials for food-grade oleic. C22 acid is derived from rapeseed and or marine oil (menhaden). Tall oil, a by-product of the kraft pulp and paper industry, is not a triglyceride and therefore does not contain glycerol (see [CARBOXYLIC ACIDS, FATTY ACIDS FROM TALL OIL](#)). Castor oil (qv) is the primary source for ricinoleic acid or 12-hydroxystearic acid when hardened. The compositions of some of these fats and oils are outlined in Table 2 (see also Table 1 of [CARBOXYLIC ACIDS, MANUFACTURE](#)).

Table 2. Typical Composition of Specific Fats and Oils, %

Lauric oils

Acid (chain length)	Coconut	Palm kernel	Tallow ^a	Palm stearine	Soybean	Tall Oil ^b	High erucic rapeseed ^c
<i>Saturated acids</i>							
caproic (C6)							
caprylic (C8)		3					
capric (C10)	7	3					
lauric (C12)	6				0.5		
myristic (C14)	50	50					
palmitic (C16)	18	18	3		0.5		
stearic (C18)	8.5	8	24	51	12		3
	3	2	20	5	4	2	1
<i>Unsaturated acids^d</i>							
palmitoleic (C16:1)			2.5				
oleic (C18:1)	6	14	43	33	25	59	18
linoleic (C18:2)	1	2	4	9	52	37	14
linolenic (C18:3)	0.5		0.5		6		7
arachidonic (C20:1)						1	10
erucic (C22:1)							46

^a Also contains ~1% of myristoleic acid (C14:1)^d.
^b Also contains ~1% of arachidic acid (C20).
^c Also contains ~0.5% each of arachidic and behenic acid (C22).
^d The number following the colon indicates the number of sites of unsaturation.

With the exception of tall oil and castor oil acids, and acids used for sodium and potassium soaps, Tables 3, 4, and 5 provide detailed production and disposition information on the U.S. triglyceride-based fatty acids. These data show a 2–3^o yr growth rate between 1985 and 1990, virtually in line with world projections, with the most significant growth occurring in the stearic and coconut acid segments.

Table 3. Saturated Fatty Acid Production and Disposition^a, 10³ t

Fatty acid	1985	1990
<i>Production</i>		
whole coconut oil-type acids ^{b, c}		
IV under 5	28.5	49.7
IV 5 or more	8.9	
fractionated and or stripped acids		
C14 and lower	22.4	30.6
C16 and C18	31.3	26.1
stearic acid		
C18 content under 75 ^o o	204.3	227.1
C18 content 75 ^o o or more	10.4	16.3
<i>Total saturated fatty acids</i>	<i>305.8</i>	<i>349.8</i>
<i>Disposition</i>		
domestic shipments	231.0	264.2
captive consumption	54.1	77.9
export shipments	4.6	
<i>Total</i>	<i>289.7</i>	<i>342.1</i>

^a Ref. 10.
^b Includes palm kernel and babassu.
^c IV Iodine value.

Table 4. Unsaturated Fatty Acid Production and Disposition^a, 10³ t

Fatty acid	1985	1990
<i>Production</i>		
oleic acid	79.8	85.9
unsaturated fatty acids other than oleic ^{b, c}		
IV 36 to under 80	60.6	46.0
IV 80 to under 130	7.1	17.5
IV 130 or more	7.5	
<i>Total unsaturated fatty acids</i>	<i>155.1</i>	<i>149.4</i>
<i>Disposition</i>		
domestic shipments	92.6	155.1
captive consumption	60.8	
export shipments	2.4	
<i>Total</i>	<i>155.9</i>	<i>155.1</i>

^a Ref. 10.
^b Includes tallow and palm acids.
^c IV Iodine value.

Table 5. Total^a Production and Disposition of All Fatty Acids, 10³ t^b

1985	1990
------	------

production	460.9	499.3
disposition		
domestic shipments	323.7	419.3
captive consumption	114.9	77.9
export shipments	7.1	
<i>Total disposition</i>	<i>445.6</i>	<i>497.2</i>

^a Sum of Tables 3 and 4.

^b Ref. 10.

Fatty acids are produced by hydrolysis (splitting), during which the triglyceride (fat or oil) reacts with water, under high temperature and pressure, to yield glycerol and free fatty acids. Historically, hydrolysis was carried out in the presence of a catalyst, but today most U.S. producers make fatty acids in a noncatalytic system. At this point in the process the fatty acids resemble the chain-length distribution of the fat or oil feedstock, and simply undergo distillation to remove color and odor impurities to make a whole cut fatty acid ready for sale. Split and distilled acids that do not undergo any further processing comprise about 10% of the U.S. market as defined by the SDA statistics in Tables 3, 4, and 5.

The majority of whole cut fatty acids are further processed for additional differentiation. Adding hydrogen (hydrogenation) removes double bonds and therefore increases stability and hardness. Acids can be either partially or fully hydrogenated depending on the properties needed, ie, melting point, reactivity, etc, for a particular application. Partially hardened (intermediate melting point) and fully hardened (high melting point) whole cut acids amount to about 45% of U.S. acid production.

Unhardened whole cut tallow and palm acids contain 40–45% oleic acid, which is derived by separation technology. This used to be done by a pressing technique; thereby the terminology *pressed* stearics. In the 1990s the separation is done using solvents and or refrigeration techniques. Oleic and pressed stearics account for about one-third of all U.S. acid production.

Whole cut acids can also undergo fractional distillation to produce fractionated acids with a high percentage content of a specific chain length, eg, 99% lauric, 95% myristic, etc. The markets for these acids are generally more specialty in nature and thereby deliver higher realization than whole cut split distilled, hydrogenated, or separated acids. Fractionated acids fill the remaining 10–12% of U.S. market demand.

Table 6 provides information on average 1991 pricing for various fatty acids as well as listing U.S. producers and typical applications for each type of acid. The U.S. fatty acid industry experienced considerable consolidation in the 1980s, whereby there are 16 active producers today, down from about 25 in the 1970s. The number of sites producing fatty acids has undergone even more extensive consolidation as the trend has been toward larger, lower cost, more fully integrated facilities.

Table 6. Oleo-Based Carboxylic Acids

Acid	Price ^a , \$ kg 1991	U.S. producers	Applications
<i>Oil specific acids</i>			
canola	0.95	Henkel Emery, Procter & Gamble, Sherex	surfactants
castor oil acids (ricinoleic, 12-hydroxystearic)	1.75	Caschem, Union Camp	lubricating greases
coconut oil acids	0.80–1.20	Dial, Henkel Emery, Procter & Gamble, Witco, Kardshamns	surfactants, soap
hydrogenated and or separated tallow-based acids	0.65	Akzo, Henkel Emery, Lonza, Procter & Gamble, Sherex, Synpro, Unichema, Witco	metallic stearates (plastic lubricants), tires, candles, crayons, cosmetics
soybean oil acids	0.90	Henkel Emery, Procter & Gamble, Witco	alkyd resins (paint)
tall oil acids			
2% or more rosin	0.55		alkyd resins, ore flotation
less than 2%	0.60	Arizona, Georgia-Pacific, Hercules, Union Camp, Westvaco	
tallow fatty acids	0.60	Akzo, Dial, Henkel Emery, Lonza, Procter & Gamble, Sherex, Synpro. Unichema, Witco	soap, lubricants, fabric softeners, asphalt emulsifiers, synthetic rubber, plastics
<i>Chain-length specific acids</i>			
capric	2.05	Akzo, Henkel Emery, Procter & Gamble, Witco	synthetic lubricants, medium-chain triglycerides
caprylic	1.85	Akzo, Henkel Emery, Procter & Gamble, Witco	synthetic lubricants, medium-chain triglycerides
caprylic-capric blend	1.30	Akzo, Dial, Henkel Emery, Procter & Gamble, Witco	synthetic lubricants, medium-chain triglycerides
lauric, 95% (dodecanoic)	1.30	Akzo, Henkel Emery, Procter & Gamble, Witco	surfactants, soap
myristic, 95% (tetradecanoic)	1.54	Henkel Emery, Procter & Gamble, Witco	esters for cosmetics, lotions
oleic	1.10	Henkel Emery, Hercules, Unichema, Witco	surfactants, lubricants, plasticizers
palmitic, 90%	1.20	Henkel Emery, Procter & Gamble, Sherex, Witco	esters for personal care products
pelargonic (nonanoic)	2.10	Henkel Emery	synthetic lubricants, plasticizers
stearic, 90%	1.00	Akzo, Henkel Emery, Lonza, Procter & Gamble, Sherex, Synpro, Unichema, Witco	alkyd resins, ore flotation

^a Ref. 11.

Because they are made from renewable natural raw materials, oleo-based fatty acids are completely biodegradable and find widespread usage in a variety of applications and industries, as is evident from Table 6.

Table 7 (12) summarizes the consumption of fatty acids by end use industry in 1987, supporting the broad base of usage and explaining the relationship with GNP.

Table 7. U.S. Consumption^{a, b} of Fatty Acids by Market Area in 1987, 10³ t

household and industrial cleaners	124
coatings and adhesives (including paints and inks)	88
personal care products (excluding toilet soap)	86
industrial lubricants, corrosion inhibitors, and oil field applications	85
plastics (excluding emulsion polymerization)	81
household fabric softeners	50
rubber (excluding emulsion polymerization)	39
emulsion polymerization	29
textiles (including textile fabric softeners)	29
foods	19
asphalt	12
paper	11
mining	8
crayons, candles, and waxes	7
miscellaneous, unassigned, and exported derivatives (including nitriles)	69
<i>Total</i>	<i>737</i>

^a Estimates are based on direct consumption of the acid or ultimate consumption of various derivatives.

^b Ref. 12.

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FATTY ACIDS FROM TALL OIL

Tall oil fatty acids (TOFA) consist primarily of oleic and linoleic acids and are obtained by the distillation of crude tall oil. Crude tall oil, a by-product of the kraft pulping process, is a mixture of fatty acids, rosin acids, and unsaponifiables (1). These components are separated from one another by a series of distillations (2). Several grades of TOFA are available depending on rosin, unsaponifiable content, color, and color stability. Typical compositions of tall oil fatty acid products are shown in Table 1 (see TALL OIL).

Table 1. Typical Fatty Acid Composition of Tall Oil Products

	CAS Registry Number	Crude tall oil, %	Crude fatty acid, %	<2% Rosin in fatty acid, %	Distilled tall oil, %
Fatty acids normalized to 100%					
C ¹ H ₃₂ O ₂	[57-10-3]	6.3	1.6	0.4	
C ₁₇ H ₃₄ O ₂	[506-12-7]	1.5	0.7	0.7	
C ₁₈ H ₃ O ₂	[57-11-4]	1.5	2.2	2.3	1.4
C ₁₈ H ₃₄ O ₂	[112-80-1]	39.8	42.3	46.4	22.9
C ₁₈ H ₃₂ O ₂	[60-33-3]	34.0	34.8	36.3	22.0
C ₁₈ H ₃₂ O ₂ (isomers)	[26764-25-0]	10.2	12.7	10.3	24.6
C ₁₉ H ₃₈ O ₂	[646-30-0]	1.2	1.1	1.1	1.1
C ₂₀ H ₃ O ₂	[25448-01-5]	4.6	4.7	2.4	28.0
Rosin acids					
		40	7	1	30
Unsaponifiables					
		8	2.5	1.5	2

At present, tall oil fatty acids are produced by six companies using 12 fractionating plants in the United States, one in Canada, 13 in Europe, two in Japan, one in New Zealand, and at least one in Russia. Worldwide crude tall oil fractionating capacity in 1988 was estimated at slightly over 1.4 million metric tons and the fractionating capacity in the United States at just over 900,000 t. Domestic production and prices of TOFA during the last 10 years are shown in Table 2. TOFA pricing is strongly dependent on soya fatty acid prices since these materials are often used in the same application.

Table 2. Production^a and Prices^b of TOFA

Year	Crude tall oil, 10 ³ t yr	TOFA, 10 ³ t yr	Approximate average price of TOFA, ¢ kg
1980	795.7	184.7	48–51
1981	799.0	184.8	37–42
1982	715.6	166.1	37–42
1983	790.9	192.5	44–46
1984	796.1	214.0	51–73
1985	785.3	186.6	80–84
1986	814.9	195.1	44–71
1987	862.1	209.5	37–53
1988	869.2	217.6	42–55
1989	901.5	219.3	55–59

^a Ref. 3.

^b Ref. 4.

Tall oil fatty acids have a variety of applications (Table 3). The largest uses of TOFA traditionally have been in coatings, primarily alkyd resins (qv) where grades of higher rosin content predominate (5). Since the 1970s their use as chemical intermediates in applications, which includes manufacture of dimer acids (qv) (6) and epoxidized TOFA esters (7), has exceeded their use in coatings. Other areas of significant use are in soaps, detergents (qv) (8), and ore flotation (qv) (9).

Table 3. U.S. Markets for Tall Oil Fatty Acids, 10⁶ kg^a

Year	Intermediate chemicals	Protective coatings	Soaps and disinfectants	Flotation	Other uses
1980	70.7	30.5	10.2	5.4	27.3
1981	77.2	34.4	10.6	7.3	32.5
1982	78.3	32.7	9.8	4.0	25.6
1983	77.0	34.5	11.0	4.1	32.7
1984	80.5	32.3	12.4	4.3	56.6
1985	62.1	27.5	13.3	4.8	43.2
1986	66.6	29.1	12.8	3.4	44.6

1987	80.1	25.9	18.0	4.5	54.5
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^a Ref. 3.

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BRANCHED-CHAIN ACIDS

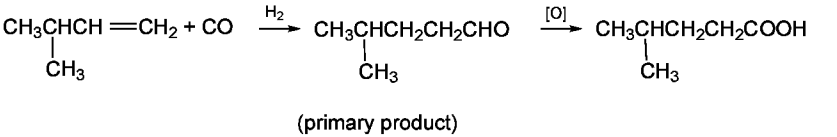
Branched-chain acids contain at least one branching alkyl group attached to the carbon chain, which causes the acid to have different physical, and in some cases different chemical, properties than their corresponding straight-chain isomers. For example, stearic acid has a melting point of about 69°C, whereas isostearic acid has a melting point of about 5°C. Some properties of commercial branched-chain acids are shown in Table 1 (1,2).

Table 1. Properties and Prices of Branched-Chain Acids

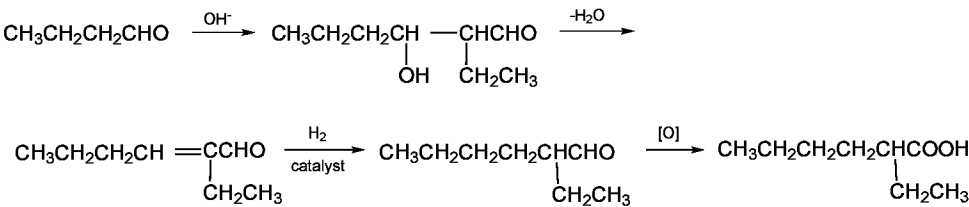
Branched-chain acid (common name)	CAS Registry Number	Molecular weight	Boiling point, °C ^a	Melting point, °C	Approximate price, \$ kg ^b	Producers in the United States
2-methylpropanoic (isobutyric) acid	[79-31-2]	88	155	−46.1	1.70	Hoechst, Eastman
2-methylbutanoic (isopentanoic) acid	[116-53-0]	102	180.3	−48	1.56	Union Carbide
3-methylbutanoic (isovaleric) acid	[503-74-2]	102	175–176.5	ca 30	4.73	Hoechst
2, 2-dimethylpropanoic (neopentanoic) acid	[75-98-9]	102	163–165	34.4	2.51	Exxon
2-ethylhexanoic acid	[149-57-5]	144	224–230	<70	1.52	Eastman, Union Carbide
mixed isomers (isononanoic) acid	[26896-18-4]	158	232–246	ca 70	1.69	Hoechst
2, 2-dimethyloctanoic (neodecanoic) acid	[129662-90-6]	172	147–150 ^c	<40	1.96	Exxon
mixed isomers (isostearic) acid	[2724-58-5]	284	192–204 ^d	ca 7	2.53	Emery, Union Camp

^a At 101.3 kPa^e unless otherwise indicated.
^b In 1990, bulk, fob.
^c At 20 kPa^e.
^d At 5 kPa^e.
^e To convert kPa to mm Hg, multiply by 7.5.

Manufacturing procedures for most branched-chain acids are well known. For example, oxo process acids are manufactured from branched-chain olefins using hydroformylation followed by oxidation (3) (see OXO PROCESS).



Neo acids are prepared from selected olefins using carbon monoxide and acid catalyst (4) (see CARBOXYLIC ACIDS, TRIALKYLACETIC ACIDS). 2-Ethylhexanoic acid is manufactured by an aldol condensation of butyraldehyde followed by an oxidation of the resulting aldehyde (5). Isopalmitic acid [4669-02-7] is probably made by an aldol reaction of octanal.



Isostearic acid is produced from dimerization and reduction of monomeric acids (6).
Branched-chain acids have a wide variety of industrial uses as paint driers (7), vinyl stabilizers (8), and cosmetic products (9). Cobalt and manganese salts of 2-ethylhexanoic acid and neodecanoic acid are used as driers for paint, varnishes, and enamels; lithium, magnesium, calcium, and aluminum salts of 2-ethylhexanoic acid are used in the formation of greases and lubricants (see DRIERS AND METALLIC SOAPS). Derivatives of isostearic acid have been used as pour point depressants in two-cycle engine oils, as textile lubricants, and in cosmetic formulations. Further industrial applications can be found (10).
The hazards of handling branched-chain acids are similar to those encountered with other aliphatic acids of the same molecular weight. Eye and skin contact as well as inhalation of vapors of the shorter-chain acids should be avoided.

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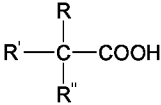
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TRIALKYLACETIC ACIDS

Trialkylacetic acids are characterized by the following structure:



in which R, R', and R'', are C_xH_{2x+1} with *x* > 1. The lowest member of the series (R = R' = R'' = CH₃) is the C₅ acid, trimethylacetic acid or 2,2-dimethylpropanoic acid (also, neopentanoic acid, pivalic acid). For higher members in the series, the products are typically mixtures of isomers, resulting from the use of mixed isomer feedstocks and the chemical rearrangements that occur in the manufacturing process.

Trialkylacetic acids have been produced commercially since the early 1960s, in the United States by Exxon and in Europe by Shell, and have been marketed as neo acids (Exxon) or as Versatic Acids (Shell). The principal commercial products are the C₈ acid and the C₁₀ acid (neodecanoic acid, or Versatic 10), although smaller quantities of other carbon numbers, such as C₆, C₇, and C₉, are also produced.

The trialkylacetic acids have a number of uses in areas such as polymers, pharmaceuticals, agricultural chemicals, cosmetics, and metal-working fluids. Commercially important derivatives of these acids include acid chlorides, peroxyesters, metal salts, vinyl esters, and glycidyl esters.

Trimethylacetic Acid

Physical Properties. 2,2-Dimethylpropionic acid [75-98-9], (CH₃)₃CCOOH, also referred to as neopentanoic acid or pivalic acid, is a solid at room temperature with a pungent odor typical of many lower molecular weight carboxylic acids. It is commercially available at a purity greater than 99.5%. Neopentanoic acid is a single isomer with a high degree of symmetry and, thus, has a relatively high melting point (+34°C, compared to -34.5°C for *n*-pentanoic acid). Physical properties of a typical commercial sample are given in Table 1.

Table 1. Physical Properties of Commercially Available Neopentanoic Acid^a

Property	Value
mp, °C	34.4
bp, °C	163–165
acid value, mg KOH/g	550
color, Pt-Co (Hazen) of molten material	50
specific gravity at 38–38°C	0.913
viscosity at 60°C, mm ² /s (cSt)	1.7
flash point, °C (Tag closed cup)	63
water, wt %	0.05
vapor pressure, kPa ^b at 60°C	1.33
solubility in water, g/100 mL H ₂ O at 25°C	2.1
heat of vaporization, kJ/kg ^c at the boiling point and 101.3 kPa ^b	423
ionization constant, <i>K</i> _a × 10 ⁻⁶ at 25°C	9.3

^a Ref. 1.

^b To convert kPa to mm Hg, multiply by 7.5.

^c To convert kJ to kcal, divide by 4.184.

Chemical Properties. Neopentanoic acid [75-98-9] undergoes reactions typical of carboxylic acids. Reactions often proceed less readily than with straight-chain acids because of the steric hindrance around the carbonyl group. However, this steric hindrance at the α-carbon results in derivatives that are typically more resistant to hydrolysis and oxidation.

Acid Chloride Formation. Neopentanoic acid can be converted to neopentanoyl chloride [3282-30-2] by reaction with thionyl chloride (2), phosgene (3), phosphorus pentachloride, phosphorus trichloride, or by the reaction with benzotrichloride in the presence of Friedel-Crafts catalysts (4). A laboratory procedure using tetramethyl-α-halogenoenamines at room temperature has also been reported (5).

Commercially, neopentanoyl chloride is often the preferred starting material for the synthesis of peroxyesters, agricultural chemicals, pharmaceuticals, esters, and other fine chemicals because the reactivity of the acid halide is generally greater than that of the acid.

Esterification. Esters of neopentanoic acid can be prepared either from the chloride or directly from the acid and alcohol. An example of the former reaction is that between neopentanoyl chloride and *tert*-butyl hydroperoxide to give *tert*-butyl peroxyneopentanoate [927-07-1], which is used as a free-radical initiator in polymerizations. For direct esterification, acid catalysts, such as sulfuric acid or toluene sulfonic acid, are used, although higher catalyst concentrations are generally required because of the lower reactivity of the acid. Methyl neopentanoate [598-98-1] has been prepared using an acid catalyst (6) or sulfonic acid cation-exchange resin (7); aromatic neopentanoate esters can be made by standard esterification procedures (8). Vinyl neopentanoate [3377-92-2] is prepared from neopentanoic acid and acetylene using zinc neopentanoate [15827-10-8] as catalyst and zinc chloride as cocatalyst (9). It can also be prepared from the acid and vinyl acetate [108-05-4] using ruthenium carbonyl as the catalyst (10). The glycol monoester can be prepared in high yields, essentially free of the diester, by reaction of the acid with ethylene oxide using an hydroxyalkylamine as the catalyst (11).

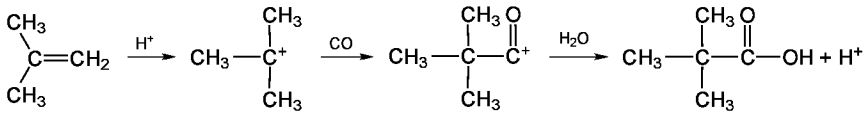
The neo acids are generally less reactive than their straight-chain counterparts. For example, neopentanoic acid reacts approximately 15 times slower than *n*-pentanoic acid (12). Greater steric hindrance, as brought about by ethyl groups, for example, results in even slower esterification rates. Once formed, however, the esters of neopentanoic acid are more resistant to hydrolysis than the corresponding linear acid esters. For example, under basic conditions, hexyl neopentanoate [5434-57-1] is hydrolyzed approximately 20 times more slowly than hexyl valerate [1117-59-5]. Under acid conditions, the difference in hydrolysis rate is a factor of 160 (13).

Reduction. 2,2-Dimethylpropanal [630-19-3] can be prepared by the reduction of neopentanoic acid using various catalysts, such as iron (14), tin or zirconium oxides (15,16), iron–chromium (17), and other reagents (18,19). The reduction of neopentanoic acid to 2,2-dimethylpropanol [75-84-3]

(neopentyl alcohol) has been accomplished using supported osmium and rhenium (20), copper–zinc or nickel (21), metal oxides (22), or sodium borohydride (23). Reduction to the alkane, 2,2-dimethylpropane [463-82-1] (neopentane), has been claimed using a copper oxide–zinc oxide catalyst (24).

Other Reactions. The anhydride of neopentanoic acid, neopentanoyl anhydride [1538-75-6], can be made by the reaction of neopentanoic acid with acetic anhydride (25). The reaction of neopentanoic acid with acetone using various catalysts, such as titanium dioxide (26) or zirconium oxide (27), gives 3,3-dimethyl-2-butanone [75-97-8], commonly referred to as pinacolone. Other routes to pinacolone include the reaction of pivaloyl chloride [3282-30-2] with Grignard reagents (28) and the condensation of neopentanoic acid with acetic acid using a rare-earth oxide catalyst (29). Amides of neopentanoic acid can be prepared directly from the acid, from the acid chloride, or from esters, using primary or secondary amines.

Manufacture. Trialkylacetic acids are prepared using variants of the Koch reaction (30), a two-stage reaction for the preparation of carboxylic acids. In the first stage, olefin, carbon monoxide, and a strong acid catalyst react to give what is commonly referred to as the complex. In the second stage, the complex is hydrolyzed to give the carboxylic acid and to regenerate the catalyst. A number of Brønsted acid catalysts have been used, including H₂SO₄, H₃PO₄, HF, and Lewis acids such as BF₃. Temperatures used depend on the choice of catalyst, and can range from –20 to +80°C, pressures used can be as high as 10 MPa (100 atm). Koch reactions have been reviewed (31). The mechanism of reaction is believed to proceed by the formation of a carbenium ion from the olefin, followed by addition of carbon monoxide to give an acylium cation. The acylium cation then reacts with water to give the carboxylic acid. This is illustrated using isobutylene [115-11-7] as the olefin, which gives neopentanoic acid as the product.



Neopentanoic acid has also been produced commercially from diisobutylene [18923-87-0], in which the first step in the reaction sequence is a cracking or depolymerization of the olefin to give isobutylene.

Commercial production of these acids essentially follows the mechanistic steps given. This is most clearly seen in the Exxon process of Figure 1 (32). In the reactor, catalyst, olefin, and CO react to give the complex. After degassing, hydrolysis of this complex takes place. The acid and catalyst are then separated, and the trialkylacetic acid is purified in the distillation section. The process postulated to be used by Shell (Fig. 2) is similar, with additional steps prior to distillation being used. In 1980, the conditions used were described as ca 40–70°C and 7–10 MPa (70–100 bar) carbon monoxide pressure with H₃PO₄–BF₃–H₂O in the ratio 1:1:1 (Shell) or with BF₃·2H₂O (Enjay) as catalyst (33).

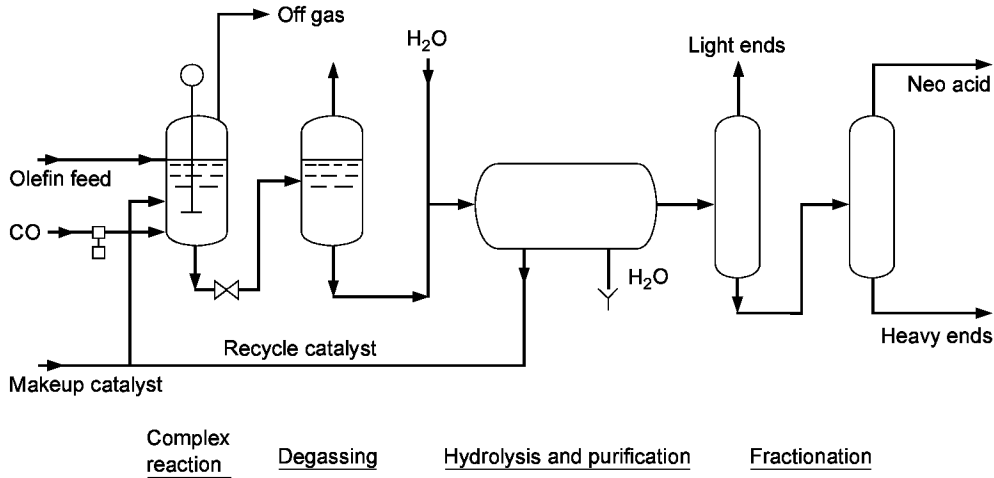


Fig. 1. Neo acid production schematic (32).

Courtesy of Hydrocarbon Processing.

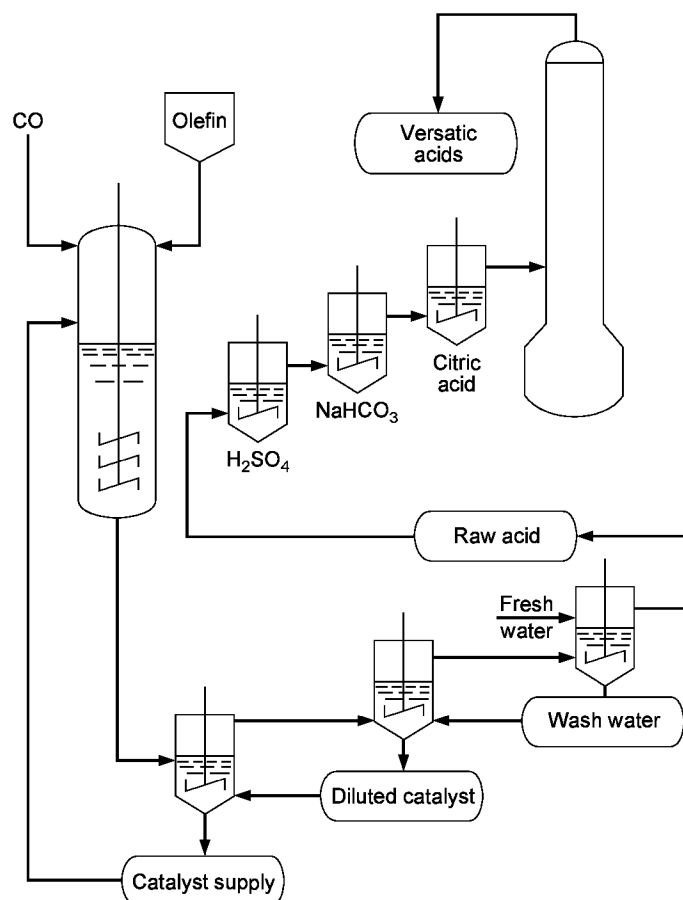


Fig. 2. Flow sheet of Shell Versatic Acid unit (33).

Work on the process for the production of these acids has continued in recent years. One patent discloses the use of zeolite catalysts (34) for the synthesis of neopentanoic acid from isobutylene. The use of a copper catalyst in a strong acid, such as sulfuric acid, operating at lower pressures, has also been claimed (35).

Economic Aspects and Shipment. Production worldwide of neopentanoic acid is estimated at 15 thousand metric tons per year. Both Shell (36) and Exxon (37) have announced expansions in capacity. Neopentanoic acid is shipped in heated tank cars, heated tank trucks, and drums.

Health and Safety Factors. Neopentanoic acid possesses low toxicity, either by ingestion (oral LD₅₀ in rats is 2.0 g/kg) or by skin absorption (dermal LD₅₀ in rabbits is 3.16 g/kg). The principal hazards associated with neopentanoic acid at ambient temperatures are from eye and skin irritation. At elevated temperatures, where concentrations of the vapor are significant, irritation of the respiratory tract can also occur. Contact with the material should be avoided.

Eye contact should be followed by flushing the eyes with large amounts of water. If irritation persists, medical attention should be obtained. Skin contact should be followed by flushing with water, using soap if available. Neopentanoic acid is combustible and will burn. Fire should be extinguished with foam, dry chemical, or water spray.

Uses.

Polymers and Resins. *tert*-Butyl peroxyneopentanoate and other peroxyesters of neopentanoic acid can be used as free-radical initiators for the polymerization of vinyl chloride [75-01-4] (38) or of ethylene [74-85-1]. These peresters have also been used in the preparation of ethylene-vinyl acetate copolymers [24937-78-8] (39), modified polyester granules (40), graft polymers of aminoalkyl acrylates with vinyl chloride resins (41), and copolymers of *N*-vinyl-pyrrolidinone [88-12-0] and vinyl acetate [108-05-4] (42). They can also be used as curing agents for unsaturated polyesters (43).

Vinyl neopentanoate is used in the preparation of adhesives and binders (44–46), optical materials for plastic lenses (47), gas permeable membranes for oxygen enrichment (48), and in coating applications (49,50).

Pharmaceuticals. Neopentanoic acid derivatives are widely used in the preparation of pharmaceuticals, eg, as a means of introducing the *tert*-butyl group into a molecule. More frequently, however, derivatives have been prepared that exploit the enhanced hydrolytic stability of the neopentanoate group. For example, when salmon calcitonin is treated with *N*-hydroxysuccinimide pivalate [42014-50-6], the resulting derivative retains the biological activity of the precursor, but gives an extended duration of activity (51).

Chloromethyl 2,2-dimethylpropionate [18997-19-8] has also been used to prepare a number of ester derivatives with improved properties compared to the nonderivatized compound. The pivaloyloxymethyl ester derivative of piperacillin [61477-96-1] is an orally administrable antibiotic agent (52) (see ANTIBIOTICS, β -LACTAMS). The pivaloyloxymethyl ester [77372-61-3] of 2-propylpentanoic acid [99-66-1] shows comparable anti-epileptic and anticonvulsant activity to the acid, but is more rapidly and uniformly absorbed in the intestinal tract than the acid itself (53). The pivaloyloxymethyl ester of 2-anilino nicotinic acid retains the analgesic and anti-inflammatory activity without the ulcerogenic activity of the free acid (54). Similarly, pivaloyloxymethyl salicylate [66195-29-7], prepared from sodium salicylate and chloromethyl pivalate, has all the favorable properties of aspirin without undesirable gastric irritation (55).

Neopentanoyl chloride has been used in the preparation of AZT (56), which is used in the treatment of acquired immune deficiency syndrome (AIDS) (see ANTIVIRAL AGENTS).

The effect of acid structure on skin penetration and skin irritation has been studied (57).

Agricultural Applications. One of the largest uses for neopentanoic acid is in the preparation of agricultural chemicals. Neopentanoic acid or its derivatives are used in the preparation of a number of commercial herbicides, such as tebuthiuron [39014-18-1], metamiltron [41394-05-2], metribuzin [21087-64-9], clomazone [81777-89-1], and oxadiazon [19666-30-9], and others (58–63). As with pharmaceuticals, the pivalate ester of a herbicide has been prepared to increase the resistance to hydrolysis, allowing the preparation of aqueous dispersions (64). A combination of a pivalic acid amide and metribuzin results in a synergism that broadens the range of applicability of the herbicide (65). The amides themselves also show nematocidal and fungicidal activity. The preparation of organotin compounds for use as miticides also involves the use of neopentanoic acid (66).

Cosmetics. Esters of neopentanoic acid are used as perfumes or perfume precursors (8,67), as liquid binders (68), and in emollient and moisturizing compositions (69).

Fuels, Lubricants, and Transmission Fluids. Polyol esters of neopentanoic acid have been used as high vacuum pumping liquids that are stable in chemically aggressive environments (70). Esters such as 6-(*p*-anilinophenoxy)hexyl pivalate are used as antioxidants for synthetic ester lubricants (71). Pivalic anhydride [1538-75-6] has been claimed as an antiknock additive for gasoline (72).

Miscellaneous Applications. The fruity odor of a series of esters, including a number of esters of neopentanoic acid, has been related to the structure of the ester, with an emphasis on pearlike odor (73). Methyl pivaloylacetate [55107-14-7], (CH₃)₃CCOOCH₂COOCH₃, prepared by condensation of methyl pivalate and methyl acetate, is used as an intermediate in the preparation of photographic chemicals (74). Degradable organic material such as aviation turbo-kerosene can be preserved by using basic zinc carboxylates, such as zinc pivalate [15827-10-8], for their biocidal activity (75) (see AVIATION AND OTHER GAS TURBINE FUELS).

C₁₀ Trialkylacetic Acids

Physical Properties. The C₁₀ trialkylacetic acids, referred to as neodecanoic acid [26896-20-8] or as Versatic 10 [52627-73-3], are liquids at room temperature. Typical physical properties for commercially available material are given in Table 2. These materials are typically mixtures of isomers, hence no structures are given throughout this section.

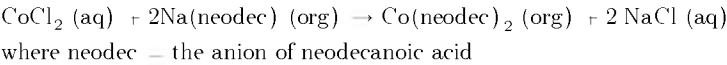
Table 2. Physical Properties of Commercially Available Neodecanoic Acid^a

Property	Value
mp, °C	< 40
bp, °C	250–257
acid value, mg KOH /g	325
color	100 (Pt /Co)
specific gravity at 20 °C	0.915
viscosity, mm ² /s (cSt)	
at 20°C	35.7
at 60°C	7
flash point, °C (Tag closed cup)	105
water, wt %	0.05
vapor pressure, kPa ^b at 60°C	0.012
solubility in water, g /100 mL H ₂ O at 25°C	0.017
heat of vaporization, kJ /kg ^c , at the boiling point and 101.3 kPa ^b	249.5
ionization constant, K _a × 10 ⁻⁶ at 25°C	4.2

^a Ref. 1.
^b To convert kPa to mm Hg, multiply by 7.5.
^c To convert kJ to kcal, divide by 4.184.

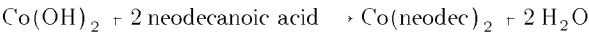
Chemical Properties. Like neopentanoic acid, neodecanoic acid, C₁₀H₂₀O₂, undergoes reactions typical of carboxylic acids. For example, neodecanoic acid is used to prepare acid chlorides, amides (76), and esters (7,11,77,78), and, like neopentanoic acid, is reduced to give alcohols and alkanes (21,24). One area of reaction chemistry that is different from the C₅ acids is the preparation of metal salts. Both neopentanoic acid and neodecanoic acid, like all carboxylic acids, can form metal salts. However, in commercial applications, metal salt formation is much more important for neodecanoic acid than it is for neopentanoic acid.

Metal Salt Formation. At least three methods are commonly used to prepare metals salts. The first of these is known as the double decomposition method.



Typically, a slight excess of acid is used, resulting in salts that are neutral or slightly acidic. This method has been applied to the preparation of zirconium salts (79).

A second method for preparing acid salts is termed fusion, represented by



In this method, a metal oxide or hydroxide is slurried in an organic solvent, neodecanoic acid is slowly added, and the mixture is refluxed to remove the water. Salts that are basic can be prepared by using less than stoichiometric amounts of acid. This method has been used in the preparation of metal salts of silver (80) and vanadium (81). The third method of preparation is similar to the fusion process, the difference is the use of finely divided metal as the starting material instead of the metal oxide or hydroxide. This method has been applied to the preparation of cobalt neodecanoate (82). Salts of tin (83) and antimony (84) have been prepared by the fusion method, starting with lower carboxylic acids, then replacing these acids with neodecanoic acid.

Manufacture. The C₁₀ trialkylacetic acids are prepared using the same process and catalysts as are used for the preparation of neopentanoic acid. For the C₁₀ acids, a branched C₉ olefin stream is typically used. Because the reaction proceeds by means of a carbenium ion mechanism, rearrangement of the olefin occurs, resulting in a C₁₀ acid composed of a large number of isomers. In addition to the carbonylation reaction, olefin dimerization and oligomerization, along with olefin disproportionation also occur, resulting in trialkylacetic acids with carbon numbers less than and greater than 10.

Economic Aspects and Shipment. The C₁₀ trialkylacetic acids are produced in volumes totaling tens of thousands of metric tons per year. The C₁₀ acids are shipped in bulk sea vessels, tank cars, tank trucks, and drums.

Health and Safety Factors. The C₁₀ trialkylacetic acids have toxicities similar to those for other neo acids: oral LD₅₀ in rats is 2.0 g /kg, and dermal LD₅₀ in rabbits is 3.16 g /kg.

The primary hazard associated with C₁₀ trialkylacetic acids is eye irritation. In contact with the eyes, the material is irritating and may injure eye tissue if not removed promptly. Any contact with the eyes should be immediately flushed with large amounts of water. Medical attention should also be obtained. For skin contact, flush with large quantities of water, using soap if available. To extinguish fires, use foam, dry chemical, or water spray.

Uses.

Polymers, Resins, and Coatings. Peroxyesters of neodecanoic acid, such as *tert*-butyl peroxyneodecanoate [26748-41-4] and α-cumyl peroxyneodecanoate [26748-47-0], constitute one of the most important uses for neodecanoic acid. These materials are used as free-radical initiators in the polymerization of vinyl chloride (85), acrylates (86), ethylene (87), styrene [100-42-5] (87), and in the copolymerization of vinyl chloride with other monomers, such as propylene [115-07-1] (88), or acrylates (89). The peroxyesters are also used as curing agents for resins (90).

Metal salts of neodecanoic acid have also been used as catalysts in the preparation of polymers. For example, bismuth, calcium, barium, and zirconium neodecanoates have been used as catalysts in the formation of polyurethane elastomers (91,92). Magnesium neodecanoate [57453-97-1] is one component of a catalyst system for the preparation of polyolefins (93); vanadium, cobalt, copper, or iron neodecanoates have been used as curing catalysts for conjugated-diene butyl elastomers (94).

The metal salts of neodecanoic acid have found wide usage as driers for paints and inks (95,96). Metal neodecanoates that are used include silver (80), cobalt (82), and zirconium (79), along with lead, copper, manganese, and zinc (see DRIERS AND METALLIC SOAPS).

Neodecanoic acid is also used as the carrier for metals in poly(vinyl chloride) heat stabilizers (qv). Metals used in this application include barium, cadmium, and zinc. Tin as the neodecanoate salt has also been claimed as a heat stabilizer for maleic anhydride (97).

Adhesion Promoters. One of the growing uses for neodecanoic acid has been in the preparation of adhesion promoters for radial tires. In this application, cobalt or nickel neodecanoate, along with other components, is used during tire manufacture to promote the adhesion or bonding of the rubber to the steel cord. The result is high adhesive strength, good thermal aging resistance and improved resistance to moisture aging (98–100).

Metal-Working and Hydraulic Fluids. In the preparation of fluids for metal-working and hydraulics, the trend has been to replace organic-based materials with aqueous-based materials. Neodecanoic acid has found application in these newer fluids as a corrosion inhibitor and a viscosity improver. For example, neodecanoic acid is used in an aqueous hydraulic fluid concentrate for corrosion inhibition and improved antiwear properties (101), in the preparation of a thickened aqueous hydraulic fluid to reduce viscosity loss (102), and in a water-soluble metal working oil to reduce corrosion (103). In a similar vein, neodecanoic acid has been used in antifreeze concentrates for corrosion inhibition (104).

Metal Extraction. As with other carboxylic acids, neodecanoic acid can be used in the solvent extraction of metal ions from aqueous solutions. Recent applications include the extraction of zinc from river water for determination by atomic absorption spectrophotometry (105), the coextraction of metals such as nickel, cobalt, and copper with iron (106), and the recovery of copper from ammoniacal leaching solutions (107).

Fuels and Lubricants. Rare-earth neodecanoates have been claimed as additives for diesel fuels that reduce the precipitation of particles and gum (108). Neodecanoic acid has also been used in the preparation of ashless detergent additives for fuels and lubricants that reduce engine deposits in internal combustion engines (109).

Electrical and Electronic Applications. Silver neodecanoate [62804-19-7] has been used in the preparation of a capacitor-end termination composition (110), lead and stannous neodecanoate have been used in circuit-board fabrication (111), and stannous neodecanoate has been used to form patterned semiconductive tin oxide films (112). The silver salt has also been used in the preparation of ceramic superconductors (113). Neodecanoate salts of barium, copper, yttrium, and europium have been used to prepare superconducting films and patterned thin-film superconductors. To prepare these materials, the metal salts are deposited on a substrate, then decomposed by heat to give the thin film (114–116) or by a focused beam (electron, ion, or laser) to give the patterned thin film (117,118). The resulting films exhibit superconductivity above liquid nitrogen temperatures.

Miscellaneous Applications. Polyamides, prepared from polyamines and neodecanoic acid, are used as wash-cycle antistatic agents (qv) (76). Salts of neodecanoic acid have been used in the preparation of supported catalysts, such as silver neodecanoate for the preparation of ethylene oxide catalysts (119), and the nickel soap in the preparation of a hydrogenation catalyst (120). Metal neodecanoates, such as magnesium, lead, calcium, and zinc, are used to improve the adherence of plasticized poly(vinyl butyral) sheet to safety glass in car windshields (121). Platinum complexes using neodecanoic acid have been studied for antitumor activity (122). Neodecanoic acid and its esters are used in cosmetics as emollients, emulsifiers, and solubilizers (77,123,124). Zinc or copper salts of neoacids are used as preservatives for wood (125).

Glycidyl and Vinyl Esters. Glycidyl neodecanoate [26761-45-5], sold commercially as GLYDEXX N-10 (Exxon) or as Cardura E10 (Shell), is prepared by the reaction of neodecanoic acid and epichlorohydrin under alkaline conditions, followed by purification. Physical properties of the commercially available material are given in Table 3. The material is a mobile liquid monomer with a mild odor and is used primarily in coatings. For example, it is used as an intermediate for the production of a range of alkyd resins (qv) and acrylics, and as a reactive diluent for epoxy resins (qv).

Table 3. Physical Properties of Commercially Available Glycidyl Neodecanoates

Property	Cardura E10 ^a	GLYDEXX N-10 ^b
color (Pt Co scale)	<60	45
density at 20°C, g mL	0.958–0.968	
water content	<0.1% mass mass	0.05 wt %
epoxy equivalent weight, g	244–256	250
flash point, °C	126 ^d	128 ^e
residual epichlorohydrin	<10 mg kg	<5 ppm
viscosity, mPa·s (cP)		
25°C	7.13	
100°C	1.31	
150°C	0.72	
vapor pressure at 37.8°C, kPa ^f	0.9	
boiling range at 101.3 kPa, °C	251–278	
freezing point, °C	< 60	
solubility in water at 20°C	0.01 % mass mass	

^a Ref. 126.
^b Ref. 127.
^c Grams of resin containing 1 g-equivalent of epoxide.
^d PMCC Pensky-Martin closed cup.
^e Tagliabue closed cup.
^f To convert kPa to mm Hg, multiply by 7.5.

Total world production of glycidyl neodecanoate is ca 7–10 thousand metric tons per year, with production by Exxon in the United States and by Shell in The Netherlands. The product is shipped in bulk or in drums and must be protected from contact with atmospheric water during storage.

Vinyl neodecanoate [26544-09-2] is prepared by the reaction of neodecanoic acid and acetylene in the presence of a catalyst such as zinc neodecanoate. Physical properties of the commercially available material, VeoVa 10 from Shell, are given in Table 4. The material is a mobile liquid with a typical mild ester odor used in a number of areas, primarily in coatings, but also in construction, adhesives, cosmetics, and a number of miscellaneous areas. Copolymerization of vinyl neodecanoate with vinyl acetate gives coating materials with excellent performance on alkaline substrates and in exterior weathering conditions.

Table 4. Physical Properties of VeoVa 10^a

Property	Value
color (Pt Co)	<15
density at 20°C, g mL	0.875–0.885
water content, % mass mass	<0.1
acid value, mg KOH g	<1.0
vinyl unsaturation, mol kg	4.85–5.10

kinematic viscosity at 20°C, mm ² s(cSt)	2.2
vapor pressure, kPa ^b	
at 30°C	<0.1
at 110°C	4.3
at 210°C	101
boiling range, °C at 13.3 kPa ^b	133–136
flash point, ^c °C	75
freezing point, °C	< 20
solubility in water at 20°C, ° o mass mass	<0.1

^a Ref. 128.
^b To convert kPa to mm Hg, multiply by 7.5.
^c PMCC Pensky-Martin closed cup closed cup.

The only producer of vinyl neodecanoate is Shell in The Netherlands, who markets the material as VeoVa 10. Production is several tens of thousands of metric tons per year. The vinyl ester is shipped in bulk or in lined drums, stabilized with 5 ppm of the monomethyl ether of hydroquinone [95-71-6] MEHQ.

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CARDIOVASCULAR AGENTS

Antiarrhythmic agents,
Antianginal agents,
Agents used in the treatment of congestive heart failure,
Antiatherosclerotic agents,
Antihypertensive agents,
Thrombolytic agents,

The cardiovascular system consists of the heart and a complex network of conduit blood vessels (aorta and vena cavae), arteries, arterioles, capillaries, venules, and veins. The function of the system is to maintain all living cells of the body with an almost constant internal and external environment. To achieve this goal there is a continuous flow of nutrients and oxygen to the cells and a continuous removal of waste products and carbon dioxide from the cells. The heart functions as a pump distributing its output to the pulmonary and peripheral circulations via this network of blood vessels and capillaries. The heart and the blood vessels, under both neural, eg, central and autonomic nervous systems (see NEUROREGULATORS), and humoral, eg, bloodborne, factors control, are also affected by the physical properties of the blood such as volume, viscosity, and the concentration of electrolytes. Under certain conditions the heart and blood vessels may malfunction causing various disorders or diseases which can lead to irreversible damage and or death. In the highly developed countries, mortality from cardiovascular disease is extremely high. In Japan, cerebrovascular disease predominates, whereas in Europe and the United States, the heart is the primary target. Cardiovascular agents are used to restore normal function to the cardiovascular system.

ANTIARRHYTHMIC AGENTS

Cardiac arrhythmias are an important cause of morbidity and mortality: approximately 400,000 people per year die from myocardial infarctions (MI) in the United States alone. Individuals with MI exhibit some form of dysrhythmia within 48 h. Post-mortem examinations of MI victims indicate that many die in spite of the fact that the mass of ventricular muscle deprived of its blood supply is often quite small. These data suggest that the cause of death is ventricular fibrillation and that the immediate availability of a safe and efficacious antiarrhythmic agent could have prolonged a number of lives. The goals of antiarrhythmic therapy are to reduce the incidence of sudden death and to alleviate the symptoms of arrhythmias, such as palpitations and syncope. Several excellent reviews of the mechanisms of arrhythmias and the pharmacology of antiarrhythmic agents have been published (1,2).

Properties of the Cardiovascular System

The Ionic Basis of Membrane Activity. Almost all living cells maintain specific internal chemical environments that are different from their external environments. In cardiac cells the principal ions involved in maintaining membrane activity are sodium, Na⁺; potassium, K⁺; chloride, Cl⁻; and calcium, Ca²⁺. The internal (i) and external (o) concentrations of these ions are: Na⁺_o 140 mM, Na⁺_i 30 mM; K⁺_o 4 mM, K⁺_i 140 mM; Cl⁻_o 104 mM, Cl⁻_i 30 mM; Ca²⁺_o 2 mM, Ca²⁺_i 100 nM. Ions diffuse through the cell membrane via protein structures, called channels, that span the membrane. The resting cell membrane is permeable to K⁺ but not to Na⁺ and the low concentration of Na⁺_i is maintained by an energy-dependent Na⁺ K⁺ adenosine triphosphatase (ATPase) pump that exchanges three Na⁺_i for two K⁺_o. The resting transmembrane potential of 90 mV, ie, the interior of the cell membrane is negative with respect to the exterior of the membrane, is determined by the ionic gradients across the membrane and the selective permeability of the membrane to these ions. When the cell depolarizes there is an increase in the permeability of the cell membrane to Na⁺_o, sodium channels are activated, and Na⁺ influx rapidly increases. The interior of the membrane becomes positive with respect to the exterior. The membrane potential at this time is +10 mV. As the cell membrane potential moves from 90 mV, becoming less negative, there is an increased inward flux of Ca²⁺ at about -60 to -50 mV accompanied by the activation of calcium channels. At +10 mV Na⁺ influx is terminated by activation of the Na⁺ K⁺ ATPase pump and Na⁺ efflux begins. The cell begins to repolarize. The first phase of repolarization is thought to result from an outward K⁺ conductance. The second phase is a result of the slow Ca²⁺ conductance; the third phase is a result of an outward K⁺ current. When the cell is fully repolarized back to its resting membrane potential, phase 4 repolarization, the ionic gradients are re-established. Calcium is removed from the cell by a Na⁺-Ca²⁺ exchange mechanism (3).

The electrical activity of individual cells can be studied using microelectrodes and recorded as transmembrane monophasic action potentials. The monophasic action potential of atrial and ventricular muscle cells and Purkinje fibers is characterized by a very rapid upstroke corresponding to phase 0, depolarization from Na⁺ influx through fast sodium channels. In atrial and ventricular muscle this is followed by a slow repolarization phase, phase 2, from a calcium inward current, and a rapid repolarization phase, phase 3, from an outward K⁺ current. Purkinje fibers have three phases of repolarization: phase 1, thought to result from an outward K⁺-conductance, a rapid repolarization; and phases 2 and 3 as in atrial and ventricular muscle. Phase 4 repolarization is the resting membrane or diastolic potential during which atrial and ventricular muscle cells and Purkinje fibers are quiescent and fully repolarized. Cells of the sinoatrial (SA) and atrioventricular (AV) nodes exhibit action potentials in which during diastole or phase 4, the cells are slowly depolarizing (diastolic depolarization). This is followed by a relatively modest rapid upstroke, phase 0 depolarization, and then a relatively slow repolarization phase, phase 3. The spontaneously and slowly depolarizing and repolarizing phases of the SA node, shown in Figure 1a (3), are characteristic of pacemaker cells.

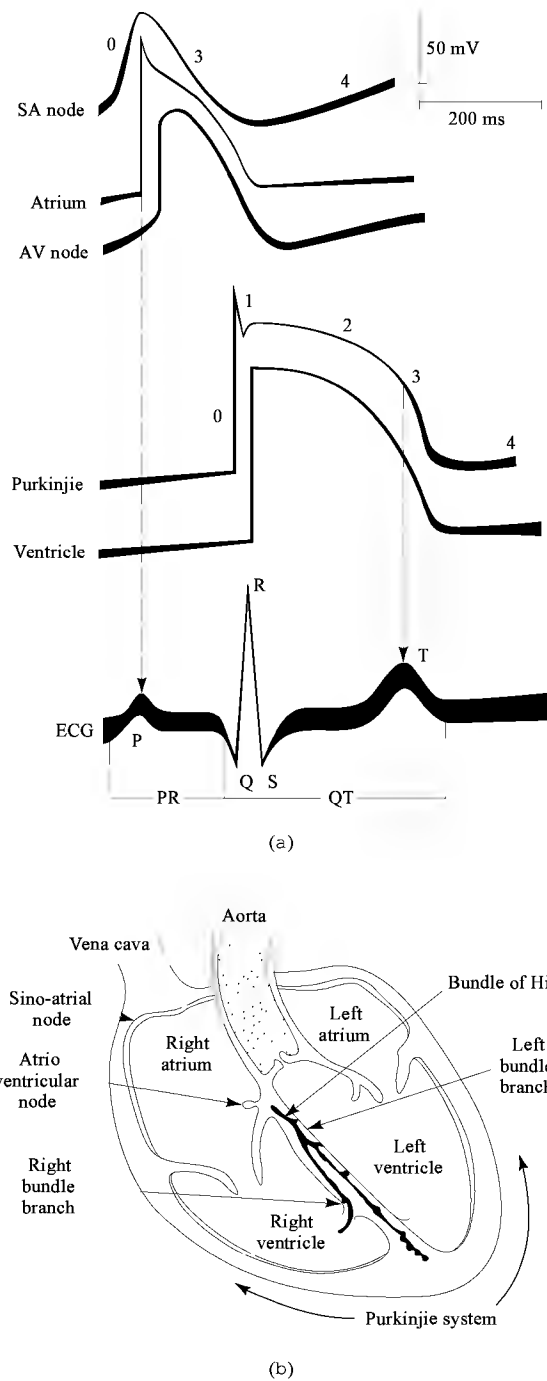


Fig. 1. (a) Myocardial cell transmembrane potentials, where the numbers and letters refer respectively to the phases and waves described in the text. ECG is electrocardiogram. (b) Conduction system of the heart.

Properties of Excitable Tissues.

Automaticity. Special cardiac cells, such as SA and AV nodal cells, His-bundle cells, and Purkinje fibers, spontaneously generate an impulse. This is the property of automaticity. Ectopic sites can act as pacemakers if the rate of phase 4 depolarization or resting membrane potential is increased, or the threshold for excitation is reduced.

Enhanced automaticity occurs in hypoxia, hypokalemia, hypercarbia, excessive sympathetic nervous system stimulation, or high concentrations of catecholamines. These conditions may lead to arrhythmias. Decreased automaticity may also lead to production of arrhythmias by enhancing ectopic activity in latent pacemakers (ectopic foci) or by altering conductivity and refractoriness in conduction pathways of myocardium.

Excitability. Excitability refers to electrical responsiveness of the heart to various stimuli by the generation of local excitatory currents, action potentials, or fibrillation.

Conductivity. Conductivity is an electrical property of excitable tissue which ensures that if one area of a membrane is excited to full activity, that area excites adjacent areas. Conduction of an impulse varies directly with the rate of development of phase 0 and the amplitude of the action potential. Phase 0 is faster, and amplitude of the action potential is greater, the more negative the transmembrane potential at the time of initiation of the impulse. Conduction velocity is faster when phase 0 is fast.

Refractoriness. The altered responsiveness of the cell membrane during recovery from previous activity is described by refractoriness. During repolarization phase 1, 2, and 3, the cell is either nonresponsive (absolute refractory period) or less responsive (effective and relative refractory periods) to the propagation of an impulse. During the absolute refractory period the cell cannot be excited regardless of the strength of the stimulating current applied, whereas during the effective refractory period the cell can be excited by applying greater stimulating currents, but the impulse is not propagated. During the relative refractory period the cell can be excited but the impulse is propagated at slower velocities, and finally during phase 4 when the cell is fully repolarized the cell can be stimulated with normal currents and the impulse is fully propagated (4).

The Cardiac Cycle. The heart (Fig. 1b) performs its function as a pump as a result of a rhythmical spread of a wave of excitation (depolarization) that excites the atrial and ventricular muscle masses to contract sequentially. Maximum pump efficiency occurs when the atrial or ventricular muscle masses contract synchronously (see Fig. 1). The wave of excitation begins with the generation of electrical impulses within the SA node and spreads through the atria. The SA node is referred to as the pacemaker of the heart and exhibits automaticity, ie, it depolarizes and repolarizes spontaneously. The wave then excites sequentially the AV node; the bundle of His, ie, the penetrating portion of the AV node; the bundle branches, ie, the branching portions of the AV node; the terminal Purkinje fibers; and finally the ventricular myocardium. After the wave of excitation depolarizes these various structures of the heart, repolarization occurs so that each of the structures is ready for the next wave of excitation. Until repolarization occurs the structures are said to be refractory to excitation. During repolarization of the atria and ventricles, the muscles relax, allowing the chambers of the heart to fill with blood that is to be expelled with the next wave of excitation and resultant contraction. This process repeats itself 60–100 times or beats per minute

in normal humans in the resting state and represents the basal rate. Highly trained healthy athletes may exhibit heart rates of 30–40 beats min⁻¹ (bradycardia), yet have similar or greater outputs to those of the average human; ie, exercise makes the heart a more efficient pump. With exercise or emotional excitement, heart rate temporarily increases above the basal rate (tachycardia), and as long as excitation begins in the SA node and follows the path described, the individual is said to have a normal sinus rhythm. An ectopic rhythm develops when excitation arises from sites other than the SA node (ectopic foci).

The electrocardiogram (ECG) is the body surface (skin) recording of the wave of electrical excitation of the heart. The ECG is the temporal summation of the electrical activity of the individual cells of the heart. The relationship of the activation of the single cells of the wave of excitation to the ECG is shown in Figure 1a. The P wave of the ECG represents the depolarization and the wave of electrical activity (conduction) over the atrial myocardium. The P–R interval represents the time necessary for conduction of impulses (propagation) through the AV node, the bundle of His, and the Purkinje fibers. The QRS complex represents the spread of the wave of excitation over the ventricular myocardium. During the QRS period the atria repolarize, and during the S–T segment, the entire ventricular mass is depolarized. The T wave represents the repolarization of the ventricular myocardial cells (4).

Cardiac arrhythmias or dysrhythmias are disturbances of the normal regular rhythm which may be caused by an abnormality in the site of impulse generation, its rate or regularity, or its propagation or conduction (1,2). The more commonly encountered cardiac arrhythmias are

Arrhythmias Originating in the Sinus Node: Sinus bradycardia; Sick sinus syndrome; Sinus tachycardia

Disorders of Impulse formation:

- Ectopic focus
- prematural atrial depolarization (contraction)
- premature junctional (AV node) depolarization
- premature ventricular depolarization
- Ectopic rhythm
- atrial ectopic tachyarrhythmia
- ventricular tachyarrhythmia
- paroxysmal tachyarrhythmia
- paroxysmal supraventricular tachyarrhythmia
- paroxysmal atrial tachycardia

Disorders of Impulse Conduction:

- Reentry mechanism
- Intranodal (AV node) reentry
- Extranodal reentry
- Reentrant tachyarrhythmia
- Atrial flutter
- Atrial fibrillation
- Ventricular tachycardia
- Ventricular fibrillation

Conduction Blocks:

The conduction of an impulse can be slowed or stopped at any point along the conduction system of the heart. Slowing of conduction is called first-degree block, block of some impulses is called second-degree block, and a block of all impulses is called third-degree block.

- Sino-atrial nodal disease
- Atrio-ventricular block

Classification of Antiarrhythmic Agents. Similarities in the electrophysiologic properties of various antiarrhythmic agents led to a proposal of classification in 1970 (5). Several other classifications have evolved since then (6–8); the most recent is the most popular (9). Classifications may be unsatisfactory for several reasons. Classifications are usually based on one primary activity and may not acknowledge differences among agents in the same group or similarities among agents in different groups, so that the electrophysiological effects of each agent may not be fully appreciated. Additionally, the electrophysiological effects are often obtained from normal myocardial preparations and the abnormalities of cellular electrophysiology which cause arrhythmias in a diseased myocardium may be uniquely related to the disease process (10). Nevertheless, antiarrhythmic agent classifications have been useful as a mnemonic device.

Class I Antiarrhythmic Agents: The Sodium Channel Blockers

The Class I antiarrhythmic agents inactivate the fast sodium channel, thereby slowing the movement of Na⁺ across the cell membrane (1,2). This is reflected as a decrease in the rate of development of phase 0 (upstroke) depolarization of the action potential (1,2). The Class I agents have potent local anesthetic effects. These compounds have been further subdivided into Classes IA, IB, and IC based on recovery time from blockade of sodium channels (11). Class IB agents have the shortest recovery times (t_{1/2} < 1 s); Class IA compounds have moderate recovery times (t_{1/2} usually <9 s); and Class IC have the longest recovery times (t_{1/2} usually >9 s).

The Class I agents decrease excitability, slow conduction velocity, inhibit diastolic depolarization (decrease automaticity), and prolong the refractory period of cardiac tissues (1,2). These agents have anticholinergic effects that may contribute to the observed electrophysiologic effects. Heart rates may become faster by increasing phase 4 diastolic depolarization in SA and AV nodal cells. This results from inhibition of the action of vagally released acetylcholine [51-84-3], which allows sympathetically released norepinephrine [51-41-2] (NE) to act on these structures (1,2).

The Class I agents have many similar side effects and toxicities. The anticholinergic side effects include dry mouth, constipation, and urinary hesitancy and retention. Common gastrointestinal (GI) side effects include nausea, vomiting, diarrhea, and anorexia. Cardiovascular adverse effects are hypotension, tachycardia, arrhythmias, and myocardial depression, especially in patients with congestive heart failure. Common central nervous system (CNS) side effects are headache, dizziness, mental confusion, hallucinations, CNS stimulation, paraesthesias, and convulsions.

Class IA Antiarrhythmic Agents. Class IA antiarrhythmic agents decrease automaticity, ie, depress pacemaker rates, especially ectopic foci rates; produce moderate depression of phase 0 depolarization and thus slow conduction in atria, A-V node, His-Purkinje system, and ventricles; prolong repolarization, ie, lengthen action potential duration; increase refractoriness; and depress excitability. These electrophysiological effects are manifested in the ECG by increases in the PR, QRS, and QT intervals.

Quinidine. Quinidine, an alkaloid obtained from cinchona bark (*Cinchona* sp.), is the dextrorotatory stereoisomer of quinine [130-95-0] (see ALKALOIDS). The first use of quinidine for the treatment of atrial fibrillation was reported in 1918 (12). The sulfate, gluconate, and polygalacturonate salts are used in clinical practice. The drug is given mainly by the oral (po) route, rarely by the intravenous (iv) route of administration. It is the most frequently prescribed po antiarrhythmic agent in the United States. The clinical uses of quinidine include suppression of atrial and ventricular extrasystoles and serious ventricular arrhythmias (1–3).

After po administration, the drug is almost completely absorbed from the GI tract and undergoes first-pass metabolism in the liver. From 70 to 87% of the dose is bioavailable, depending on the salt used, and 10 to 20% of the absorbed dose is free in the circulation. The drug binds mainly to albumin, but also enters the red blood cell and binds to hemoglobin. At equilibrium, the concentrations in red blood cells and plasma may be equal. Peak plasma concentrations are achieved in 1–4 h depending on the salt used. Therapeutic plasma concentrations are 3–6 µg mL⁻¹; toxic reactions occur above 8 µg mL⁻¹. The metabolites of quinidine are 3-hydroxyquinidine, quinidine-*N*-oxide, 2'-oxyquinidine, and *O*-desmethylquinidine. Only 3-hydroxyquinidine has antiarrhythmic activity and achieves plasma levels about one-third of those achieved by the unchanged drug. The kidneys excrete 75–90% of the dose as

metabolites, sulfonate or glucuronate conjugates, and the remainder as unchanged drug (1,2).

The cardiovascular adverse effects associated with quinidine therapy are hypotension and tachycardia, both of which are related to its α -adrenoceptor blocking actions. The tachycardia may be a reflex adjustment to the fall in blood pressure or may also be a direct action of the drug on sympathetic nerve terminals leading to an increased release of NE. Quinidine also produces ringing in the ears (cinchonism) (1,2).

Procainamide. Procainamide hydrochloride is a benzamide, synthesized to prolong the therapeutic effects of the local anesthetic procaine [59-46-1] (13) (see ANESTHETICS). The drug is effective in a wide range of supraventricular and ventricular arrhythmias (14).

Procainamide may be administered by iv, intramuscular (im), or po routes. After po dosing, 75–90% of the drug is absorbed from the GI tract. About 25% of the amount absorbed undergoes first-pass metabolism in the liver. The primary metabolite is *N*-acetylprocainamide (NAPA) which has almost the same antiarrhythmic activity as procainamide. This is significant because the plasma concentration of NAPA relative to that of procainamide is 0.5–2.5. In terms of drug metabolism there are two groups of patients: those that rapidly acetylate and those that slowly acetylate procainamide. About 15–20% of the drug is bound to plasma proteins. Peak plasma concentrations are achieved in 60–90 min. Therapeutic plasma concentrations are 4–10 $\mu\text{g mL}$. Plasma half-lives of procainamide and NAPA, which are excreted mainly by the kidneys, are 2.5–4.5 and 6 h, respectively. About 50–60% is excreted as unchanged procainamide (1,2).

About 30% of the patients on chronic procainamide dosing develop a systemic lupuslike syndrome consisting of arthralgia, myalgia, skin rash, and fever. Patients who are slow acetylators phenotypes may be prone to this condition. Some may exhibit pleuropneumonic involvement and hepatomegaly (1,2).

Disopyramide. Disopyramide phosphate, a phenylacetamide analogue, is a racemic mixture. The drug can be administered po or iv and is useful in the treatment of ventricular and supraventricular arrhythmias (1,2). After po administration, absorption is rapid and nearly complete (83%). Binding to plasma protein is concentration-dependent (35–95%), but at therapeutic concentrations of 2–4 $\mu\text{g mL}$, about 50% is protein-bound. Peak plasma concentrations are achieved in 0.5–3 h. The drug is metabolized in the liver to a mono-*N*-dealkylated product that has antiarrhythmic activity. The elimination half-life of the drug is 4–10 h. About 80% of the dose is excreted by the kidneys, 50% is unchanged and 50% as metabolites; 15% is excreted into the bile (1,2).

Class IB Antiarrhythmic Agents. Class IB antiarrhythmic agents produce less inhibition of the inward sodium current than Class IA agents. In normal myocardial tissue, phase 0 may be unaffected or minimally depressed. However, in ischemic or infarcted tissue, phase 0 is depressed. Myocardial tissue exposed to Class IB agents exhibits decreased automaticity, shortened action potential duration, ie, shortened repolarization, and shortened refractory period. Excitability of the myocardium is not affected and conduction velocity is increased or not modified. The refractory period is shortened less than its action potential duration, thus the ratio of refractory period to action potential duration is increased by these agents. The net effect is increased refractoriness. The PR and QT intervals of the ECG are shortened and the QRS interval is unchanged (1,2).

Lidocaine. Lidocaine hydrochloride, an anilide, was originally introduced as a local anesthetic in 1943 and found to be a potent antiarrhythmic in 1960. The compound is a reverse amide of procainamide. Lidocaine is generally considered to be the drug of choice in the treatment of ventricular arrhythmias and those originating from digitalis glycoside toxicity (1,2,15–17).

Lidocaine is given iv. Po dosing is inadequate because after rapid absorption, about 70% of the drug undergoes extensive first-pass metabolism in the liver to monoethylglycine xylide (MEGX) and glycine xylide (GX). MEGX has 80–100% and GX 10–25% of the antiarrhythmic potency of lidocaine, respectively. Plasma concentrations of MEGX may be 50–200% and GX 10–100% those of lidocaine. Lidocaine is 60–80% bound to plasma protein. Time to peak plasma concentration depends on the rate of IV dosing but is usually achieved in 45–90 seconds. Therapeutic plasma concentrations are 1.5–5.0 $\mu\text{g mL}$, and concentrations above 5 $\mu\text{g mL}$ may be toxic. The elimination half-life after a bolus iv dose is 8 min; the elimination half-life after a 24 h iv infusion is about 100 min. The drug is eliminated by the kidneys. Ten percent is unchanged and the remainder is in the form of inactive metabolites (1,2).

Phenytoin. Phenytoin sodium is sodium diphenylhydantoin [630-93-3] which is structurally related to the barbiturates. It was originally introduced as an anticonvulsant (18) (see HYPNOTICS, SEDATIVES, AND ANTICONVULSANTS) and later found to have antiarrhythmic properties (19), although not approved by the FDA for any arrhythmic indications. Phenytoin is effective in the treatment of ventricular arrhythmias associated with acute MI and with digitalis toxicity (20). It is not very effective in treatment of supraventricular arrhythmias (20).

Phenytoin's absorption is slow and variable yet almost complete absorption eventually occurs after po dosing. More than 90% of the drug is bound to plasma protein. Peak plasma concentrations are achieved in 1.5–3 h. Therapeutic plasma concentrations are 10–20 $\mu\text{g mL}$ but using fixed po doses, steady-state levels are achieved in 7–10 days. Phenytoin is metabolized in the liver to inactive metabolites. The plasma half-life is approximately 22 h. Phenytoin is excreted primarily in the urine as inactive metabolites and <5% as unchanged drug. It is also eliminated in the feces and in breast milk (1,2). Prolonged po use of phenytoin may result in hirsutism, gingival hyperplasia, and hypersensitivity reactions evidenced by skin rashes, blood dyscrasias, etc (1,2).

Mexilitene. Mexilitene hydrochloride, a phenyl ether, is a po active congener of lidocaine. It is used clinically for suppression of ventricular arrhythmias (1,2).

Mexilitene is well absorbed from the GI tract and less than 10% undergoes first-pass hepatic metabolism. In plasma, 60–70% of the drug is protein bound and peak plasma concentrations are achieved in 2–3 h. Therapeutic plasma concentrations are 0.5–2.0 $\mu\text{g mL}$. The plasma half-life of mexilitene is 10–12 h in patients having normal renal and hepatic function. Toxic effects are noted at plasma concentrations of 1.5–3.0 $\mu\text{g mL}$, although side effects have been noted at therapeutic concentrations. The metabolite, *N*-methylmexilitene, has some antiarrhythmic activity. About 85% of the drug is metabolized to inactive metabolites. The kidneys excrete about 10% of the drug unchanged, the rest as metabolites. Excretion can also occur in the bile and in breast milk (1,2).

Moricizine. Moricizine, a phenothiazine derivative, was synthesized and developed in Russia, where it has been in general use since 1971. FDA approval of the new drug application (NDA) for use in the United States was granted in 1991. It is effective against atrial and ventricular arrhythmias (1,2,21).

Following po administration moricizine is completely absorbed from the GI tract. The drug undergoes considerable first-pass hepatic metabolism so that only 30–40% of the dose is bioavailable. Moricizine is extensively (95%) bound to plasma protein, mainly albumin and α_1 -acid glycoprotein. The time to peak plasma concentrations is 0.42–3.90 h. Therapeutic concentrations are 0.06–3.00 $\mu\text{g mL}$. Using radiolabeled moricizine, more than 30 metabolites have been noted but only 12 have been identified. Eight appear in urine. The sulfoxide metabolite is equipotent to the parent compound as an antiarrhythmic. Elimination half-life is 2–6 h for the unchanged drug and known metabolites, and 84 h for total radioactivity of the labeled drug (1,2).

Tocainide. Tocainide is a po active primary amine analogue of lidocaine. It consists of the (*S*)-(–) and the more active (*R*)-(+) enantiomers. The drug is effective in the treatment of ventricular arrhythmias, especially those following acute myocardial infarctions (1,2,22).

Tocainide is rapidly and well absorbed from the GI tract and undergoes very little hepatic first-pass metabolism. Unlike lidocaine which is ~30% bioavailable, tocainide's availability approaches 100% of the administered dose. Food delays absorption and decreases plasma levels but does not affect bioavailability. Less than 10% of the drug is bound to plasma proteins. Therapeutic plasma concentrations are 3–9 $\mu\text{g mL}$. Toxic plasma levels are >10 $\mu\text{g mL}$. Peak plasma concentrations are achieved in 0.5–2 h. About 30–40% of tocainide is metabolized in the liver by deamination and glucuronidation to inactive metabolites. The metabolism is stereoselective and the steady-state plasma concentration of the (*S*)-(–) enantiomer is about four times that of the (*R*)-(+) enantiomer. About 50% of the tocainide dose is eliminated by the kidneys unchanged, and the rest is eliminated as metabolites. The elimination half-life of tocainide is about 15 h, and is prolonged in patients with renal disease (1,2,23).

Some rare toxic effects that may result from tocainide therapy are a lupus-like syndrome, skin rash, pulmonary complications, and hematologic abnormalities, eg, agranulocytosis (1,2,24).

Class IC Antiarrhythmic Agents. Class IC antiarrhythmic agents have marked local anesthetic effects. They slow the rapid inward sodium current producing marked phase 0 depression and slow conduction. Action potential duration of ventricular muscle is increased, ie, prolonged repolarization, but decreased in the His-Purkinie system by these agents. The effects on the ECG are increased PR interval, marked prolongation of the

QRS interval, and increased QT interval (1,2).

Encainide. Encainide hydrochloride, a benzamide derivative, is effective in the treatment of ventricular arrhythmias and refractory ventricular tachycardia (1,2).

Encainide is almost completely absorbed from the GI tract. Food may delay absorption without altering its bioavailability. The drug is rapidly metabolized in 90% of the patients to two principal metabolites, O-demethylencaïnide (ODE) and 3-methoxy-O-demethylencaïnide (MODE), while the other 10% metabolize encainide slowly with little or no ODE or MODE formed. Encainide, ODE, and MODE are extensively protein bound: 75–80% for encainide and ODE and 92% for MODE. Peak plasma concentrations are achieved in 30–90 min. Therapeutic plasma concentrations are very low; the concentrations of ODE and MODE are approximately five times those of encainide. The findings with the metabolites are significant because ODE is 2–10 times and MODE, 1–4 times more effective than encainide as antiarrhythmics. The half-lives for encainide in fast and slow metabolizers is 1–2 h and 6–12 h, respectively. The elimination half-life for ODE is 3–4 h and for MODE 6–12 h in fast metabolizers. Excretion occurs through the liver and kidneys (1,2).

Adverse effects of encainide therapy are dose-related. Diplopia and a bad taste in the mouth have been reported (1,2,25).

Flecainide. Flecainide acetate, a fluorobenzamide, is a derivative of procainamide, and has been reported to be efficacious in suppressing both supraventricular and ventricular arrhythmias (26–29). The drug is generally reserved for patients with serious and life-threatening ventricular arrhythmias. Flecainide depresses phase 0 depolarization of the action potential, slows conduction throughout the heart, and significantly prolongs repolarization (30). The latter effect indicates flecainide may possess some Class III antiarrhythmic-type properties (31).

Flecainide is well absorbed and 90% of the po dose is bioavailable. Binding to plasma protein is only 40% and peak plasma concentrations are attained in about 1–6 h. Three to five days may be required to attain steady-state plasma concentrations when multiple doses are used. Therapeutic plasma concentrations are 0.2–1.0 µg mL. Flecainide has an elimination half-life of 12–27 h, allowing twice a day dosing. The plasma half-life is increased in patients with renal failure or low cardiac outputs. About 70% of the flecainide in plasma is metabolized by the liver to two principal metabolites. The antiarrhythmic potency of the meta-O-dealkylated metabolite and the meta-O-dealkylated lactam, relative to that of flecainide is 50 and 10%, respectively. The plasma concentrations of the two metabolites relative to that of flecainide are 3–25%. Flecainide is mainly excreted by the kidneys, 30% unchanged, the rest as metabolites or conjugates; about 5% is excreted in the feces (1,2).

Propafenone. Propafenone hydrochloride, an arylketone, is structurally similar to the β-adrenoceptor blocking agents. It has been in use in the former West Germany since 1977 and was introduced in the United States in 1990. Its effects may result from a combination of weak calcium channel blocking, weak nonselective β-adrenoceptor blocking, and sodium channel blocking activity. Propafenone is effective in treating supraventricular tachyarrhythmias, ventricular ectopic beats, and ventricular arrhythmias. It is the most frequently prescribed medication for ventricular arrhythmias in Europe (32).

About 97% of po dose is absorbed from the GI tract. The drug undergoes extensive first-pass hepatic metabolism and only 12% of the po dose is bioavailable. More than 95% is protein bound and peak plasma concentrations are achieved in 2–3 h. Therapeutic plasma concentrations are 0.064–1.044 µg mL. The drug is metabolized in the liver to 5-hydroxypropafenone, which has some antiarrhythmic activity, and to inactive hydroxymethoxy propafenone, glucuronides, and sulfate conjugates. Less than 1% of the po dose is excreted by the kidney unchanged. The elimination half-life is 2–12 h (32).

Patients taking propafenone may experience a metallic taste after ingesting the drug (32).

Indecainide. Indecainide hydrochloride is a po active antiarrhythmic agent that received FDA approval in 1989, but it has not been marketed as of this writing. Chemically, it is 9-[3-(isopropylamino)propyl]fluorine-9-carboxamide [74517-78-5]. The drug has potent activity against premature ventricular complexes (PVCs) and ventricular tachycardias. Indecainide has no effect on sinus node function, atrial or ventricular effective refractory periods (32,33).

Therapeutic blood levels range from 0.3–0.9 µg mL. Mean elimination halflife is 9 h (32).

Class I Antiarrhythmic Agents Under Development.

Lorcainide. Lorcainide hydrochloride, introduced in the former West Germany in 1981, is investigational in the United States. The compound is an acetanilide derivative having local anesthetic properties. It is available in po and iv formulations and is an effective treatment for suppressing supraventricular extrasystoles, repetitive atrial tachycardias, and ventricular arrhythmias. Lorcainide is a long-acting agent allowing for twice a day dosing schedules (32).

Absorption is complete and bioavailability is about 100% at steady state during continuous po dosing. There is extensive hepatic first-pass metabolism to nordorcinide and hydroxylated metabolites. Nordorcinide is equipotent and equieffective to lorcainide in antiarrhythmic activity. Therapeutic plasma concentrations are 0.15–0.50 µg mL. The elimination half-life of lorcainide is about 8 h and that of nordorcinide, 26 h (32). Lorcainide has low cardiovascular toxicity (32).

Pirmenol. Pirmenol hydrochloride, a pyridine methanol derivative, is a racemic mixture. It has Class IA antiarrhythmic activity, ie, depression of fast inward sodium current, phase 0 slowing, and action potential prolongation. The prolongation of refractory period may be a Class III property. This compound has shown efficacy in converting atrial arrhythmias to normal sinus rhythm (34,35).

Class II Antiarrhythmic Agents: The β-Adrenoceptor Blocking Agents

β-Adrenoceptor blocking agents (β-adrenoceptor blockers) are often called β-blockers. However, the former term more accurately describes the way in which these drugs act. They bind selectively to β-adrenoceptors in a competitive and reversible way to antagonize the responses of neurally-released, humoral or exogenously-administered sympathomimetic amines. Some of these Class II agents have local anesthetic properties and are described as "quinidinelike" because their cardiac electrophysiological properties are similar to those of Class IA agents (1,2,11).

β-Adrenoceptors have been subdivided into β₁- and β₂-adrenoceptors. A third subset called nontypical β-adrenoceptors or β₃-adrenoceptors have been described but are still the subject of debate. In terms of the interactions with various subsets of β-adrenoceptors, some antagonists are nonselective in that they antagonize the effects of activation of both β₁- and β₂-adrenoceptors, whereas others are selective for either β₁- or β₂-adrenoceptors. β₁- and β₂-adrenoceptors coexist in almost all organs but generally, one type predominates. The focus herein is on the clinically relevant β₁-adrenoceptor-mediated effects on heart and on β₂-adrenoceptor-mediated effects on smooth muscles of blood vessels and bronchioles, the insulin-secreting tissue of the pancreas, and skeletal muscle glycogenolysis for side effects profile (36).

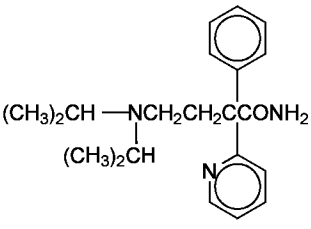
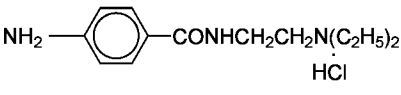
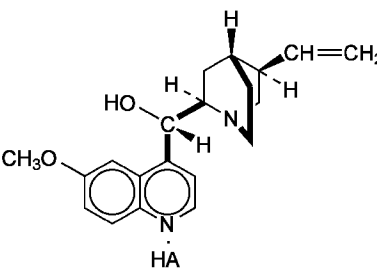
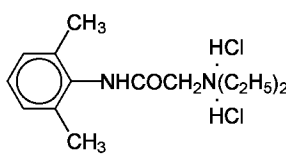
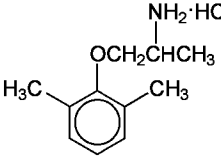
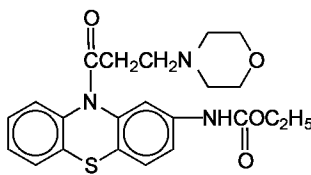
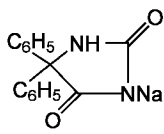
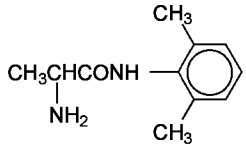
Agents that preferentially block β₁-adrenoceptor-mediated effects on the heart, resulting in reduced rate, force, and velocity of cardiac contractility, are classified as cardioselective β-adrenoceptor blockers. Thus these agents would be beneficial in patients having arrhythmias that are present with peripheral vascular disease, asthma, and insulin-dependent diabetes because the β-adrenoceptors in the organs involved are of the β₂-adrenoceptor subtype and blocking the β₂-adrenoceptors would worsen the disease states. However, cardioselectivity may be lost at high doses or concentrations of the β-adrenoceptor blocker. Some β-adrenoceptor blocking agents have local anesthetic properties resulting from membrane stabilizing and have effects on cardiac cells similar to those described for the Class I antiarrhythmic agents, ie, they reduce the rate of rise of the action potential without affecting action potential duration. This effect may be apparent at concentrations in excess of their therapeutic range (36).

Some β-adrenoceptor blockers have intrinsic sympathomimetic activity (ISA) or partial agonist activity (PAA). They activate β-adrenoceptors before blocking them. Theoretically, patients taking β-adrenoceptor blockers with ISA should not have cold extremities because the drug produces minimal decreases in peripheral blood flow (smaller increases in resistance). In addition, these agents should produce minimal depression of heart rate and cardiac output, either at rest or during exercise (36).

There have been a number of long-term trials with various β-adrenoceptor blockers in patients surviving acute MI (37–39) that demonstrated a reduction in mortality, sudden death, and nonfatal re-infarctions. The term cardioprotective has been used to describe this effect for the drugs studied. The

mechanism of the cardioprotective effect is not understood and whether this property applies to all β-adrenoceptor blockers is unknown. Timolol [26839-75-8], C₁₃H₂₄N₄O₃S, metoprolol, atenolol, and propranolol have been shown to possess this cardioprotective property (37–39) (Table 1).

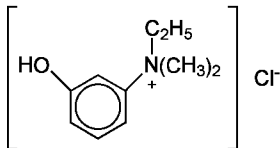
Table 1. Antiarrhythmic Agents

Generic name	CAS Registry Number	Molecular formula	Trade name	Structure
Class IA agents (Sodium channel blockers)				
disopyramide phosphate	[22059-60-5]	C ₂₁ H ₂₉ N ₃ O	Norpace	
procainamide hydrochloride	[614-39-1]	C ₁₃ H ₂₂ ClN ₃ O	Procan, Pronestyl	
quinidine gluconate ^a quinidine sulfate ^b	[7054-25-3] [6591-63-5]	C ₂₀ H ₃₂ N ₂ O ₉ C ₄₀ H ₅₀ N ₄ O ₈ S	Duraquin, Cin-QuinQuindex, Quinora	
Class IB agents (Sodium channel blockers)				
lidocaine hydrochloride	[73-78-9]	C ₁₄ H ₂₃ ClN ₂ O · H ₂ O	Xylocaine, Dalcaine	
mexiletine hydrochloride	[5370-01-4]	C ₁₁ H ₁₈ ClNO	Mexitil	
moricizine	[31883-05-3]	C ₂₂ H ₂₅ N ₃ O ₄ S	Ethmosin	
phenytoin sodium	[630-93-3]	C ₁₅ H ₁₁ N ₂ NaO ₂	Dilantin	
tocainide	[41708-72-9]	C ₁₁ H ₁₁ N ₂ O	Tonocard	
Class IC agents (Sodium channel blockers)				
encainide hydrochloride	[66794-74-9]	C ₂₂ H ₂₀ ClN ₂ O ₂	Encaid	

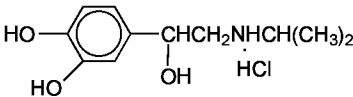
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flecainide acetate	[54143-56-5 /	C ₁₇ H ₂₀ F N ₂ O ₃	Tambocor		
indacainide hydrochloride	[73681-12-6 /	C ₂₀ H ₂₄ N ₂ O	Decabid		
propafenone hydrochloride	[34183-22-7 /	C ₂₁ H ₂₈ ClNO ₃			
lorcainide hydrochloride	[58934-46-6 /	C ₂₂ H ₂₈ Cl ₂ N ₂ O	Other Class I agents		
pimrenol hydrochloride	[61477-94-9 /	C ₂₂ H ₃₁ ClN ₂ O			
acebutolol hydrochloride	[37517-30-9 /	C ₁₈ H ₂₀ ClN ₂ O ₄	Class II agents (β-Adrenoceptor blockers) Sectral		
bopindolol	[62658-63-3 /	C ₂₃ H ₂₈ N ₂ O ₃			
carteolol hydrochloride	[51781-21-6 /	C ₁ H ₂₅ ClN ₂ O ₃	Cartrol		
esmolol hydrochloride	[81161-17-3	C ₁ H ₂ ClNO ₄	Brevibloc		

	/			
flestolol sulfate	[88844-73-9 /]	C ₁₅ H ₂₂ FN ₃ O ₄ ·H ₂ S O ₄		
metoprolol tartrate	[56392-17-7 /]	C ₁₅ H ₂₅ NO ₃	Lopressor	
propranolol hydrochloride	[319-98-9]	C ₁ H ₂₂ ClNO ₂	Inderal	
amiodarone	[1951-25-3]	C ₂₅ H ₂₀ I ₂ NO ₃	<i>Class III agents</i> Cordarone	
bretylum tosylate	[61-75-6]	C ₁₈ H ₂₄ BrNO ₃ S	Bretylol	
clofilium phosphate	[60379-03-3 /]	C ₂₁ H ₃₀ ClNO ₄ P		
sotalol hydrochloride	[959-24-0]	C ₁₂ H ₂₁ ClN ₂ O ₃ S		
verapamil hydrochloride	[152-11-4]	C ₂₇ H ₃₀ ClN ₂ O ₄	<i>Class IV agents</i> Calan	
alinidine hydrobromide	[33178-86-8 /]	C ₁₂ H ₁₄ BrCl ₂ N ₃	<i>Class V agents</i>	
atropine sulfate	[5908-99-6]	C ₃₄ H ₄₈ N ₂ O ₁₀ S	<i>Autonomic agents</i>	
edrophonium chloride	[116-38-1]	C ₁₀ H ₁₁ ClNO	Tensilon	

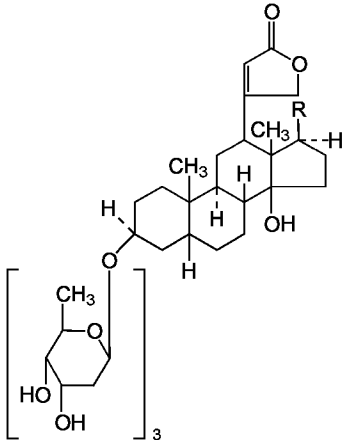
isoproterenol hydrochloride [51-30-9] C₁₁H₁₈ClNO₃ Isuprel, Norisodrine



phenylephrine hydrochloride [61-76-7] C₉H₁₄ClNO₂

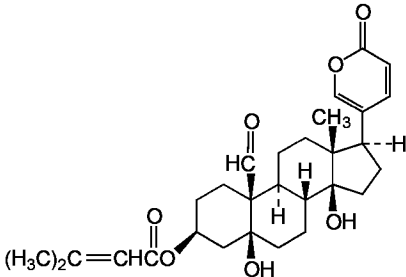


digitoxin^c digoxin^d [71-63-6] C₄₁H₆₄O₁₃ C₄₁H₆₄O₁₄ *Digitalis glycosides*
[20830-75-5] Cardigin, Crystodigin,
Digisidin,
/ Linidigin Lanoxin

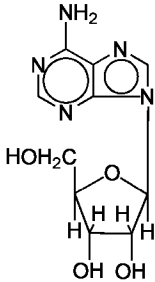


acrihellin [67696-82-6] C₂₉H₃₈O₇

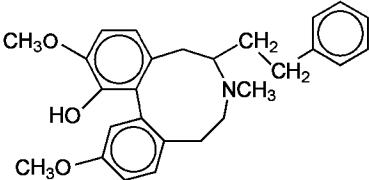
Unclassified agents



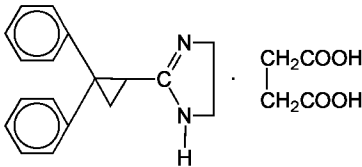
adenosine [58-61-7] C₁₀H₁₃N₅O₄ Adenocard



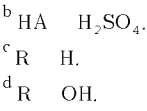
asocainol [77400-65-8] C₂₇H₃₁NO₃



cifenline succinate [100678-32-8] C₂₂H₂₄N₂O₄ Cipralan



^a HA = gluconic acid.



In addition to the properties described, β-adrenoceptor blockers may be lipophilic or hydrophilic in nature depending on the extent to which they partition between water and organic solvents. Lipophilic agents more readily cross the blood—brain barrier and are more likely to produce adverse CNS effects, eg, drowsiness, lassitude, impaired concentration, hallucinations, and nightmares. Lipophilic agents are eliminated by the liver and blood levels, duration of action, and toxicological potential may be increased in the presence of liver disease. Hydrophilic agents, on the other hand, are eliminated by the kidneys and blood levels, duration of action, and toxic potential may be increased in the presence of impaired kidney function. These factors have prompted the search for β-adrenoceptor blockers that have a balanced clearance profile, wherein the drugs are equally excreted by the liver and kidneys and elimination is not affected by dysfunction of either organ (36).

Prolonged exposure of β-adrenoceptor agonists down-regulates β-adrenoceptors, ie, their number decreases and they become less responsive. On the other hand, prolonged exposure to β-adrenoceptor antagonists (those without ISA) upregulates β-adrenoceptors, ie, their numbers increase and they become more responsive. Therefore, patients on β-adrenoceptor blocker therapy should be withdrawn from this medication gradually (40).

The properties of β-adrenoceptor blockers that contribute to antiarrhythmic effects are antagonism of neural humoral β-adrenergic activity, and antagonism of catecholamine-mediated electrophysiological properties, ie, increase refractory period and decrease in the rate of diastolic depolarization, ie, decrease automaticity and slow atrioventricular conduction (1,2).

Propranolol. Propranolol hydrochloride, considered the prototype of the β-adrenoceptor blocking agents, has been in use since 1964. It is a nonselective, highly lipid-soluble β-adrenoceptor blocker having no ISA. It is a mixture of (+) and (−) enantiomers, and the (−) enantiomer is the active moiety. The local anesthetic effects of propranolol are equipotent to those of lidocaine [137-58-6], C₁₄H₂₂N₂O, (see ANESTHETICS). Therapeutic effects include termination of catecholamine-induced arrhythmias, conversion of SA nodal tachycardias (including flutter and fibrillation) and AV nodal tachyarrhythmias to normal sinus rhythm, digitalis-induced arrhythmias, and ventricular arrhythmias (1,2). The drug also has cardioprotective properties (37,39).

Greater than 90% of a po dose of propranolol is absorbed from the gastrointestinal (GI) tract. Propranolol undergoes extensive first-pass hepatic metabolism and only 25% of the parent compound is bioavailable. Peak plasma concentrations are achieved in about 2 h. About 93% is bound to plasma protein. The drug is metabolized by O-dealkylation, side-chain oxidation, glucuronide conjugation, and ring oxidation. The ring hydroxylated metabolites, eg, 4-hydroxypropranolol, have β-adrenoceptor blocking activity. Only 1–4% of administered drug is excreted unchanged in the urine. Its elimination half-life is 3–4 h. The (+) enantiomer of propranolol is eliminated more slowly than the (−) enantiomer (1,2).

Toxic effects of propranolol are related to its blocking β-adrenoceptor blocking actions. They include cardiac failure, hypotension, hypoglycemia, and bronchospasm. Propranolol is lipophilic and crosses the blood—brain barrier. Complaints of fatigue, lethargy, mental depression, nightmares, hallucinations, and insomnia have been reported. GI side effects include nausea, vomiting, diarrhea, and constipation (1,2).

Acebutolol. Acebutolol hydrochloride is a hydrophilic, cardioselective β-adrenoceptor blocker that has about 1–25 the potency of propranolol in this regard. The drug has moderate ISA and weak membrane stabilizing activities. It is approved for the treatment of hypertension and ventricular arrhythmias, especially PVCs. Acebutolol should produce minimal depression of heart rate because of its ISA (32).

Acebutolol is well absorbed from the GI tract. It undergoes extensive hepatic first-pass metabolism. Bioavailability of the parent compound is about 40%. The principal metabolite, N-acetylacebutolol, has antiarrhythmic activity and appears to be more cardioselective. Binding to plasma proteins is only 26%. Peak plasma concentrations of acebutolol are achieved in 2.5 h, 3.5 h for N-acetylacebutolol. The elimination half-lives of acebutolol and its metabolite are 3–4 and 8–13 h, respectively. The compounds are excreted by the kidneys (30–40%) and by the liver into the bile (50–60%). About 40% of the amount excreted in the urine is unchanged acebutolol, the rest as metabolites (32).

In addition to the toxic effects indicated for propranolol, acebutolol may produce hair loss and elevate antinuclear antibody titers (32).

Esmolol. Esmolol hydrochloride, an ultrashort acting cardioselective β₁-adrenoceptor blocker having no ISA or membrane stabilizing activity, is minimally lipid-soluble. The β-adrenoceptor blocking activity is 0.07 that of propranolol. It is used primarily for short-term management of supraventricular tachyarrhythmias, including atrial fibrillation and flutter, perioperative supraventricular arrhythmias, and postoperative hypertension and acute myocardial ischemia (41).

Esmolol is iv administered. Maximal β-adrenoceptor blockade occurs in 1 min. Its elimination half-life is about 9 min. Full recovery from β-adrenoceptor blockade is within 30 min after stopping the infusion. The therapeutic plasma concentrations are 0.4–1.2 μg mL. It is metabolized by hydrolysis in whole blood by red blood cell esterases resulting in the formation of a primary acid metabolite and free methanol. The metabolite is pharmacologically inactive. The resulting methanol levels are not toxic. Esmolol is 55% bound to plasma protein, the acid metabolite only 10%. Less than 2% of parent drug and the acid metabolite are excreted by the kidneys. Plasma levels may be elevated and elimination half-lives prolonged in patients with renal disease (41).

Because of its brief half-life and minimal lipid solubility, the side effects of esmolol are transient and include hypotension, cold extremities, dyspnea (from bronchospasms), bradycardia, nausea, vomiting, and headaches (41).

Other β-Adrenoceptor Blocking Agents. Several other β-adrenoceptor blocking agents are in development as antiarrhythmic agents. These include carteolol, flestolol, and bopindolol (see Table 1).

Carteolol hydrochloride, a hydrophilic, long-acting, nonselective β-adrenoceptor blocker, has ISA and minimal membrane stabilizing activity. The drug has antihypertensive, antiarrhythmic, and antianginal effects (stable exertional angina) (42). About 78–83% of a po dose of carteolol is absorbed from the GI tract. The rest is excreted in the feces. Carteolol is 80–90% bioavailable. It undergoes hepatic first-pass metabolism. About 40–68% of the oral dose is excreted in the urine as unchanged carteolol, the rest as metabolites or conjugated compounds (3–18%). The primary metabolite in humans is 8-hydroxy-carteolol. Four other metabolites have been identified in animal studies (42). The side effects and toxicity of carteolol are similar to those associated with β-adrenoceptor blocking agent therapy (42).

Flestolol sulfate is a nonselective, ultrashort acting β-adrenoceptor blocker. It has no ISA and produces weak inhibition of the fast sodium channel. The drug is under clinical investigation for supraventricular tachyarrhythmias, unstable angina, and acute MI. In humans, flestolol has hemodynamics and electrophysiologic effects similar to those of other β-adrenoceptor blockers. The pharmacokinetics of flestolol are similar to those of esmolol. It is 50 times more potent than esmolol and the elimination half-life is 7.2 min. Recovery from β-adrenoceptor blockade is 30–45 min after stopping iv infusions. The drug is hydrolyzed by tissue esterases and no active metabolites of flestolol have been identified (41).

Bopindolol is a long-acting, nonselective β-adrenoceptor blocker. It has mild membrane stabilizing activity and ISA. *In vivo*, the compound is hydrolyzed to its active metabolite. Because of this prodrug feature the onset of action is slower than other available β-adrenoceptor blockers. Preliminary pharmacokinetic studies indicate that the compound is well absorbed, is 70% bioavailable, and peak plasma levels are achieved in about 2 h. Whereas its elimination half-life is 4–8 h, β-adrenoceptor blocking action (~40%) is still apparent after 48 h. The drug is being studied in hypertension, angina, and arrhythmias (43).

Class III Antiarrhythmic Agents

The Class III antiarrhythmic agents markedly prolong action potential duration and effective refractory period of cardiac tissue. The QT interval of the ECG is markedly prolonged.

Amiodarone. Amiodarone, an iodinated benzofuran derivative that has structural similarities to the thyroid hormones (qv), was originally

The side effects and toxic reactions to verapamil include upper GI upset, constipation, dizziness, headaches, flushing and burning, edema, hypotension, bradycardia, and various conduction disturbances. Verapamil has negative inotropic activity and may precipitate heart failure in patients having ventricular dysfunction (1,2).

Class V Antiarrhythmic Agents: Selective Bradycardic Agents

Class V agents have antiarrhythmic activity in sinus tachyarrhythmias. The bradycardia produced by these agents results from effects on the SA node to reduce the slope of phase 4 diastolic depolarization and prolonging SA node action potential duration. The effects are not mediated by a vagal sensitizing action, a muscarinic or cholinergic effect, a β -adrenoceptor blocking effect, or an effect on calcium or sodium channels. It appears that these agents may restrict anionic membrane currents (74). As of this writing only one compound has been studied that has this property.

Alinidine. Alinidine bromide (see Table 1) is the N-allyl analogue of clonidine, an α -adrenoceptor agonist. Alinidine produces greater effects on rate than on contractile force (75). This distinguishes alinidine from the calcium channel antagonists, the cholinergic agents, or Class I antiarrhythmic agents. The compound is being evaluated in patients having hyperkinetic heart syndrome (76,77), coronary artery disease (78,79), angina (80,81), sinus tachycardia, and acute MI (82).

Autonomic Drugs Used in the Treatment of Arrhythmias

Drugs that mimic or inhibit the actions of neurotransmitters released from parasympathetic or sympathetic nerves innervating the heart may also be used to treat supraventricular bradyarrhythmias, heart block, and supraventricular tachyarrhythmias. Those used in the treatment of arrhythmias may be found in Table 1.

Edrophonium. Edrophonium chloride is a rapid acting anticholinesterase agent. It inhibits the enzyme cholinesterase that inactivates acetylcholine and thus prolongs the actions of acetylcholine at sites of cholinergic innervation, eg, the vagus and the heart. Thus its pharmacologic and electrophysiologic effects are similar to those of acetylcholine. The heart rate is slowed by slowing diastolic depolarization and decreasing automaticity in SA and AV nodes. It slows conduction in the AV node. In atrial muscle, action potential duration is decreased (effective refractory period is decreased) and conduction velocity is increased. It can be used to terminate supraventricular tachycardias that do not respond to maneuvers to stimulate the vagus. The actions of edrophonium are transient (about 10 min duration). Adverse effects are salivation, sweating, miosis, and GI disturbances. Sinus arrest and complete heart block are also possible with the use of edrophonium (83,84).

Atropine. Atropine sulfate is an alkaloid obtained from the Belladonna plant (see ALKALOIDS). It is an anticholinergic agent and is a competitive inhibitor of acetylcholine, the neurotransmitter released from the vagus nerve which innervates the heart. Vagal stimulation and acetylcholine slows the heart rate by decreasing phase 4 diastolic depolarization in SA and AV nodes. It decreases the duration of the action potential of atrial muscle but not of ventricular muscle. Acetylcholine slows conduction velocity in AV node but increases conduction velocity in atrial muscle. This is reflected by a prolonged PR interval in the ECG. Atropine effects are opposite those of acetylcholine and it is useful for the treatment of bradyarrhythmias by blocking the actions of vagal stimulation. It increases conduction velocity in the AV node (85).

Atropine is well absorbed orally and can be administered parenterally. About 50% of an administered dose is metabolized in the liver, the rest is excreted in the urine unchanged. About 77–94% of an administered dose is excreted in the urine. The pharmacological half-life of atropine is about 2–3 h (85).

Adverse effects with atropine therapy include dry mouth, myosis, loss of visual accommodations, constipation, and urinary retention. The drug can also produce flushing, hyperthermia, delirium, tachycardia, and exacerbate glaucoma (85).

Isoproterenol. Isoproterenol hydrochloride is a nonselective β -adrenoceptor agonist that is chemically related to NE. It mimics the effects of stimulation of the sympathetic innervation to the heart which are mediated by NE. It increases heart rate by increasing automaticity of the SA and AV nodes by increasing the rate of phase 4 diastolic depolarization. It is used in the treatment of acute heart block and supraventricular bradyarrhythmias, although use of atropine is safer for bradyarrhythmias following MI (86).

Isoproterenol may also be used in cardiac arrest. It is often administered as an iv or intracardiac bolus along with sustained external cardiac massage to circulate the drug and stimulate the SA pacemaker to resume automaticity (86).

Isoproterenol is given sublingually or by iv. It is metabolized by monoamine oxidase and catechol-O-methyltransferase in brain, liver, and other adrenergically innervated organs. The pharmacological effects of isoproterenol are transient because of rapid inactivation and elimination. About 60% is excreted unchanged. Adverse effects using isoproterenol therapy include nervousness, hypotension, weakness, dizziness, headache, and tachycardia (86).

Phenylephrine. Phenylephrine hydrochloride is an α_1 -adrenoceptor agonist. Phenylephrine produces powerful vasoconstrictor and hypertensive responses. This results in baroreceptor activation of a reflex bradycardia and thus is useful in the treatment of supraventricular tachyarrhythmias. Unlike epinephrine [51-43-4], the actions of which are relatively transient, phenylephrine responses are more sustained (20 min after iv dosing and 50 min after subcutaneous dosing) (86).

Digital Glycosides in the Treatment of Arrhythmias

The digitalis glycosides (see Table 1) play an important role in the treatment of supraventricular tachyarrhythmias, particularly atrial fibrillation. These agents have direct and indirect (vagomimetic or vagal sensitizing effects) actions on various parts of the heart. In general, the therapeutic effect is to decrease AV conduction by increasing refractoriness of the AV node and to slow the heart. Thus the ventricle does not respond to the tachycardic rates of the SA node or ectopic sites in the atrium (87).

Digoxin. Digoxin is one of the digitalis glycosides used in the treatment of supraventricular tachyarrhythmias. A po dose of tablet or elixir is 60–85% absorbed from the GI tract. Food delays absorption but the total amount of drug absorbed is unchanged. Onset of therapeutic effect is 0.5–2 h for po and 5–30 min for iv preparations. About 25% of an administered dose is protein-bound. Peak serum levels are observed in 45 min to 2 h. About 90% of the po dose is excreted unchanged and about 10% is excreted as metabolites. Excretion is primarily through the kidneys. About 60–90% of an administered dose is excreted in seven days. Patients having impaired kidney function have higher blood levels and longer elimination half-lives of digoxin (87).

Adverse reactions to digoxin include anorexia, vomiting, diarrhea, dizziness, headaches, visual disturbances, and cardiac arrhythmias. Allergic reaction such as urticaria, skin eruptions, fever, and edema have been reported (87).

Digitoxin. Digitoxin is a cardiac glycoside obtained from *Digitalis purpurea*. Digitoxin is indicated in the treatment of atrial flutter, atrial fibrillation, and supraventricular tachycardia. Its electrophysiologic and adverse effects are similar to those described for digoxin (87).

Because digitoxin is a nonpolar, lipophilic glycoside, absorption from the GI tract is complete. About 90% of the drug in plasma is tightly bound to protein. It is metabolized in the liver to many metabolites, including digoxin which is the only pharmacologically active metabolite. The drug is excreted via the bile into feces. The elimination half-life of digitoxin is seven to nine days (87).

Unclassified Approved Antiarrhythmic Agents

Adenosine, 6-amino-9- β -ribofuranosyl-9-*H*-purine (see Table 1), is an endogenous nucleoside found in all cells of the body. Its ubiquitousness suggests that adenosine functions as an autocoid and that its actions are mediated by specific receptors on the plasma membranes of all cells.

Adenosine is not active orally, but administered as an iv bolus drug adenosine rapidly eliminates supraventricular tachycardias within 1–2 min after dosing. The drug slows conduction through the AV node. Adenosine is rapidly removed from the circulation by uptake into red blood cells and vascular endothelial cells. Thus the plasma half-life is less than 10 s. Adenosine is rapidly metabolized to inosine or adenosine monophosphate and becomes part of the body pool for synthesis of adenosine-triphosphate.

Adenosine in large doses produces vasodilation resulting in facial flushing, lightheadedness, dizziness, and hypotension. Shortness of breath and

introduced as a coronary vasodilator and antianginal agent in Europe in 1967 (44,45). It was subsequently found to have potent antiarrhythmic actions (46). The compound has a wide spectrum of antiarrhythmic activity against supraventricular and ventricular arrhythmias (47,48).

The electrophysiological effects of amiodarone may be a composite of several properties. In addition to prolonging action potential duration and refractory period in all tissues of the heart, the compound is an effective sodium channel blocker (49), calcium channel blocker (50), and a weak noncompetitive β -adrenoceptor blocking agent (51). Amiodarone slows the sinus rate, markedly prolongs the QT interval, and slightly prolongs the QRS duration (1,2).

Amiodarone dilates arteriolar vascular smooth muscle, especially coronary arteries, and thus exhibits antianginal effects. Its effects on the peripheral vasculature to decrease resistance leads to a decrease in left ventricular stroke work and a decrease in myocardial oxygen consumption. The drug rarely produces hypotension that requires discontinuation of the drug (1,2).

The GI absorption of the drug after po administration is slow and variable with estimates ranging from 20–55%. Once absorbed, 96% of the drug is bound to plasma proteins and other tissues on the body. Whereas peak plasma concentrations may be achieved in 3–7 h, the onset of antiarrhythmic action may occur in 2–3 days or more. This may result, in part, from distribution to and concentration of the drug in adipose tissue, liver, spleen, and lungs. Therapeutic plasma concentrations are 1–2 $\mu\text{g mL}$, although there appears to be no correlation between plasma concentration and antiarrhythmic activity. The plasma half-life after discontinuation of the drug varies from 13–103 days. The drug is metabolized in the liver and the principal metabolite is desethylamiodarone. The primary route of elimination is through the bile. Less than 1% of the unchanged drug is excreted in the urine. The drug can also be eliminated in breast milk and through the skin (1,2).

Amiodarone exhibits many prominent adverse side effects. The drug is deposited as yellowish-brown microcrystals in almost every organ. About 10% of the patients observe halos or have blurred vision resulting from deposits in the cornea. About 10–25% of the patients exhibit photodermatitis because of deposits in the skin with 5% developing a grayish blue skin discoloration. Pulmonary inflammation and fibrosis with concomitant loss of pulmonary function occurs in 10–15% of patients. Because iodine accounts for about 40% of the molecular weight of amiodarone, thyroid function may be increased or decreased upon prolonged use. Neurological reactions include tremors, staggering gait and impaired ambulation, ataxia, paresthesias, and sleep disturbances (vivid dreams or nightmares). About 10% of the patients become constipated (1,2).

Bretylum. Bretylum tosylate, a bromobenzyl quaternary ammonium compound, is a relatively simple molecule having a complex pharmacological profile. The drug was originally introduced as an antihypertensive agent (52) and later found to possess antiarrhythmic antifibrillatory properties (53,54). The electrophysiological effects of bretylum are prolongation of action potential duration (delayed repolarization), effective refractory period, and elevation of fibrillation threshold of the myocardium (1,2). Immediately upon iv injection the drug is taken up into postganglionic adrenergic nerves releasing norepinephrine [51-41-2] (NE), $\text{C}_8\text{H}_{11}\text{NO}_3$, resulting in an increase in heart rate and in hypertension because of an increase in vascular resistance (sympathomimetic actions). Subsequently the drug exhibits adrenergic neuronal blocking action and prevents the release of NE from the same postganglionic nerve terminals. The latter activity is the pharmacological basis of its antihypertensive effects. Bretylum is primarily indicated for life-threatening ventricular tachycardias and fibrillation (55–57).

Because bretylum is poorly absorbed from the GI tract (~10%), it is administered iv or im. Very little drug is protein bound in plasma. Bretylum is taken up by an active transport mechanism into and concentrated in postganglionic nerve terminals of adrenergically innervated organs. Peak plasma concentrations after im injections occur in about 30 min. Therapeutic plasma concentrations are 0.5–1.0 $\mu\text{g mL}$. Bretylum is not metabolized and >90% of the dose is excreted by the kidneys as unchanged drug. The plasma half-life is 4–17 h (1,2).

Adverse effects with bretylum include hypotension, nausea, vomiting, parotid gland tenderness, and arrhythmogenesis (1,2).

Sotalol. Sotalol hydrochloride was introduced as a competitive, nonselective β -adrenoceptor blocker (58) and its potency has been estimated at 1/10–1/50 (59,60) to 1/100 (61) that of propranolol. Its electrophysiological effects consist of increased action potential duration (prolonged repolarization) with no change in the upstroke velocity of phase 0 depolarization (no effect on the sodium current) (62). The electrophysiological effects of sotalol are independent of its β -adrenoceptor blocking actions (63) because the (–)-isomer, which is devoid of the β -adrenoceptor blocking action, produces effects similar to those of the (+)-isomer and the (–), (+)-racemate on increasing refractoriness. Sotalol will antagonize catecholamine-induced effects on the myocardium. The compound produces an increase in myocardial contractile force that is not adrenergically mediated (no ISA) (64). The compound is effective in the treatment of supraventricular tachycardias (65), suppression of PVCs (66), nonsustained ventricular tachycardias (67), and inducible sustained ventricular tachycardias (68).

Sotalol is rapidly and almost completely (>90%) absorbed. Bioavailability of absorbed drug is 89–100%. Peak plasma levels are achieved in 2–4 h. Sotalol is 50% bound to plasma proteins. Plasma half-life of the compound is about 5.2 h. No metabolites of sotalol have been identified indicating little metabolism. The drug is excreted mainly by the kidneys (80–90%) and about 10% is eliminated in the feces. The plasma half-life is prolonged in patients having renal failure. Kinetics of the compound are not affected by changes in liver function (1,2). Sotalol has all the adverse effects of β -adrenoceptor blockers including myocardial depression, bradycardia, transient hypotension, and proarrhythmic effects (1,2).

Other Class III Antiarrhythmic Agents. Clofilium phosphate is a benzene-butanaminium derivative that has highly specific Class III antiarrhythmic activity. It is orally active, has a rapid onset of action, and a reasonably long duration of antiarrhythmic activity. In preliminary clinical studies, clofilium has shown efficacy against spontaneous ventricular tachycardias (69).

Class IV Antiarrhythmic Agents: The Calcium Antagonists

The calcium antagonists have also been known as calcium channel blockers, calcium entry blockers, slow channel blockers, or calcium channel antagonists. The term calcium antagonist is the accepted descriptive term for this class of drugs. The World Health Organization (WHO) has subdivided the calcium antagonists into six classes (70) represented by Roman numerals. The phenylalkylamines, eg, verapamil, constitute Class I; dihydropyridines, eg, nifedipine, Class II; benzothiazepines, eg, diltiazem, Class III; flunarizinelike compounds, Class IV; prenylaminelike compounds, Class V; and other agents in Class VI.

The general biochemical mechanism for contraction in cardiac, skeletal, or smooth muscle is dependent on the availability of a critical intracellular calcium concentration. Calcium enters cells by a variety of mechanisms. In cardiac cells, calcium enters through slow channels that are 100 times more selective for calcium than sodium. This occurs during phase 2 (plateau phase of repolarization) of the action potential, at which time there is a slow inward current of calcium through these channels. Phase 2 repolarization is depressed or shortened by calcium antagonists. In the SA and AV nodes, the calcium antagonists inhibit slow response action potentials, slow conduction, and prolong the PR interval of the ECG. The only calcium antagonist approved for antiarrhythmic indications is verapamil [52-53-9], $\text{C}_{27}\text{H}_{38}\text{N}_2\text{O}_4$, although diltiazem $\text{C}_{22}\text{H}_2\text{N}_2\text{O}_4\text{S}$, [42399-41-7], and others have similar electrophysiologic properties and may be useful antiarrhythmic agents (1,2).

Verapamil. Verapamil hydrochloride (see Table 1) is a synthetic papaverine [58-74-2], $\text{C}_{20}\text{H}_{21}\text{NO}_4$, derivative that was originally studied as a smooth muscle relaxant. It was later found to have properties of a new class of drugs that inhibited transmembrane calcium movements. It is a (–), (+) racemic mixture. The (–)-isomer has local anesthetic properties and may exert effects on the fast sodium channel and slow phase 0 depolarization of the action potential. The (+)-isomer affects the slow calcium channel. Verapamil is an effective antiarrhythmic agent for supraventricular AV nodal reentrant arrhythmias (VI-2) and for controlling the ventricular response to atrial fibrillation (1,2,71–73).

After po dosing, verapamil's absorption is rapid and almost complete (>90%). There is extensive first-pass hepatic metabolism and only 10–35% of the po dose is bioavailable. About 90% of the drug is bound to plasma proteins. Peak plasma concentrations are achieved in 1–2 h, although effects on AV nodal conduction may be apparent in 30 min (1–2 min after iv administration). Therapeutic plasma concentrations are 0.125–0.400 $\mu\text{g mL}$. Verapamil is metabolized in the liver and 12 metabolites have been identified. The principal metabolite, norverapamil, has about 20% of the antiarrhythmic activity of verapamil (3). The plasma half-life after iv infusion is 2–5 h whereas after repeated po doses it is 4.5–12 h. In patients with liver disease the elimination half-life may be increased to 13 h. Approximately 50% of a po dose is excreted as metabolites in the urine in 24 h and 70% within five days. About 16% is excreted in the feces and about 3–4% is excreted as unchanged drug (1,2).

chest pressure is seen in about 10^o % of the patients.

Antiarrhythmic Agents Under Development. Three potential antiarrhythmic agents (Table 1) are in various stages of development.

Asocainol. Asocainol, a dibenzazonine derivative, has sodium channel (Class I) and calcium channel (Class IV) blocking activity that accounts for the antiarrhythmic activity. Preliminary studies indicate that the compound is effective against ventricular arrhythmias (88). Additional studies are needed to establish efficacy, toxicological potential, and pharmacokinetic profile.

Cifenline. Cifenline succinate, also known as cibenzoline, is an imidazoline derivative that is under development in the United States as an antiarrhythmic agent. It is a sodium channel blocker (Class IA), markedly prolongs action potential duration (Class III), and has calcium channel blocking activity (Class IV) (89). Cifenline has efficacy against ventricular arrhythmias (90–92). The pharmacokinetic profile and toxicological potential of cifenline is not well established at this writing (93).

Achrihellin. Achrihellin, a synthetic cardiac glycoside, is an ester of the corresponding aglycon of hellebrin [13289-18-4], a bufodienolide. The compound has electrophysiological properties of the cardiac glycosides and antiadrenergic properties. These properties suggest utility in the treatment of supraventricular tachycardias (94).

Antiarrhythmic Drug Therapy Problems

Drugs used to treat and prevent cardiac arrhythmias have relatively small therapeutic dose to toxic dose ratios. Whereas antiarrhythmic drugs have been shown to be effective in the treatment of a wide variety of arrhythmias, worsening of ventricular arrhythmias (proarrhythmia) is a frequent and serious side effect of antiarrhythmic drugs and may lead to sudden death (11,94,95). Table 2 lists the incidence of worsening of arrhythmias by several antiarrhythmic agents. The effects on decreasing mortality have not been demonstrated. To determine whether these agents have effects on mortality, the National Heart, Lung, and Blood Institute in 1985 conducted a one-year preliminary trial in 10 medical centers called "The Cardiac Arrhythmia Pilot Study" (CAPS). The safety and efficacy of four antiarrhythmic agents were compared to a placebo in 502 post-acute myocardial infarction (MI) patients having premature ventricular complexes (PVCs) and nonsustained ventricular tachycardias. The results indicated that encainide suppressed PVCs 79^o %, flecainide 83^o %, moricizine 66^o %, imipramine 52^o %, and placebo 37^o %. Encainide, flecainide, and moricizine were considered safe and effective for suppressing PVCs in post-MI patients (96). The National Institutes of Health (NIH) began a follow-up study in 1987 called "The Cardiac Arrhythmia Suppression Trial" (CAST), using 1500 patients, to determine whether encainide, flecainide, and moricizine would decrease the incidence of sudden cardiac death in post-MI patients when compared to a placebo. In 1989 an interim review of CAST revealed a significantly higher incidence (3.6-fold) of deaths in the encainide or flecainide groups than in the placebo group. Encainide and flecainide were removed from the study and the trial continued with moricizine and placebo treatments. The moricizine placebo trial of CAST was also terminated in mid-1991 because there was a higher incidence of deaths in the moricizine-treated group than in the placebo group. The Food and Drug Administration (FDA) Cardiorenal Advisory Committee recommended that encainide, flecainide, and other Class IC agents were to be used for life-threatening or symptomatic arrhythmias and not for nonlife-threatening arrhythmias. It was additionally concluded that Class IA and IB drug monographs should have some type of warning and description of the CAST results including the statement: "No benefit with respect to mortality has been shown for any antiarrhythmic drug." Class IA and IB agents were not restricted to use for life-threatening arrhythmias (97).

Table 2. Incidence of Worsening of Arrhythmias

Antiarrhythmic agent	Incidence, ^o %
<i>Class IA</i>	
quinidine sulfate	16.1–17.0
procainamide hydrochloride	7.5–12.2
disopyramide phosphate	5.7–6.3
aprinidine hydrochloride	13.2–13.3
<i>Class IB</i>	
mexilitene hydrochloride	10.3–10.9
tocainide hydrochloride	9.2–23.1
<i>Class IC</i>	
encainide hydrochloride	25.0
lorcainide	7.9
flecainide	14.3
propafenone	11.3
<i>Class II</i>	
propranolol hydrochloride	6.5–14.6
metoprolol	15.6–18.5

ANTIANGINAL AGENTS

Angina pectoris is the principal symptoms of ischemic heart disease, which manifests itself as a dramatic, terrorizing, pressing poststernal pain. It occurs suddenly and can be severe. The location and character of the pain may vary but often radiates from the sternum to the left shoulder and over the flexor surface of the left arm to the tips of the medial fingers. It can be induced by exercise, anxiety, overeating, or stress and is often relieved quickly by rest. Other factors, such as decreased oxygen carrying capacity of the blood, or reduced aortic pressure may be involved. The attack may be transient and damage to the ischemic myocardium may be minimal or it may result in an acute MI and or death. It is usually accompanied by ST segment changes in the ECG depending on the condition. The pain results from temporary ischemia of the myocardium when the oxygen supply is insufficient to meet the metabolic demands, either by a decrease in blood supply or an exceedingly large increase in oxygen requirements of the myocardium or both. For a drug to be efficacious in angina it should improve myocardial oxygen supply (increase blood flow) or reduce myocardial oxygen consumption or have both actions.

There are different classifications of angina. Stable angina is defined as angina in which no change in frequency, duration, or precipitating causes of the attacks have occurred in the past 30 days. Duration of pain is less than 15 min and occurs on effort or exertion. Unstable angina is defined as angina in which there is a progressive changing pattern, ie, an increase in frequency, severity, and or duration of pain (crescendo angina), or there is a new onset of angina present for less than 30 days. Unstable angina may occur at rest or on exertion. Variant angina (Prinzmetal's angina) is angina resulting from coronary artery spasm (98).

Nitrate Therapy in Angina

Nitrates may produce relief of angina although differently in the various subsets of angina. For example, in stable exertional angina, the action of nitrates on decreasing myocardial oxygen demand is greater than that on relaxing coronary arteries. In unstable angina, nitrates reduce left ventricular wall tension and dilate eccentric stenotic coronary arteries, whereas in Prinzmetal's angina the primary effect of nitrates is to relax coronary vasospasm (98).

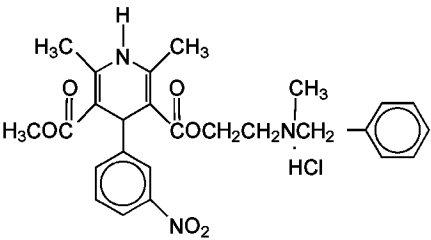
The precise mechanism of nitrate action is not clearly understood and may be a combination of many factors. The basic pharmacologic action of nitrates is a relaxation of most vascular smooth muscle, eg, vascular, bronchial, gastrointestinal, uretal, uterine, etc. Vascular smooth muscle relaxation is a

direct effect that is not mediated by adrenergic receptors or endothelium. The nitrates react with sulphhydryl containing receptors in vascular smooth muscles to form *S*-nitrosothiol, which in turn activates guanylate cyclase to form cyclic-guanosine monophosphate [7665-99-8] (cGMP), C₁₀H₁₂N₅O₇P (99).

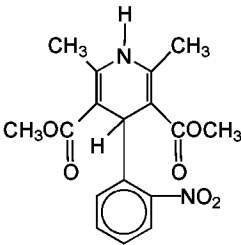
Nitrates may release prostacyclin [35121-78-9], C₂₀H₃₂O₅, from the endothelial lining of the vasculature and thereby relax vascular smooth muscle. Prostacyclin is a potent endogenous vasodilator and inhibitor of platelet aggregation. Nitrates may be effective in relieving anginal pain by redistributing coronary blood flow to the ischemic myocardium following coronary artery dilation, or by improving the perfusion of the subendocardium. Reduction of myocardial oxygen demand has been proposed as part of the mechanism for relieving angina. In support of this hypothesis are the observations that nitrates also relax venous capacitance vessels, cause venous pooling, and decrease venous return to the heart. These actions on the venous side of the circulation reduce preload, left ventricular volume, and ventricular wall tension. Combined with the action on arteriolar resistance to reduce afterload and increase cardiac output, nitrates reduce the external work of the ventricles and, in turn, decrease oxygen requirements of the myocardium (98,99). Nitrate antianginal agents are shown in Table 3.

Table 3. Antianginal Agents

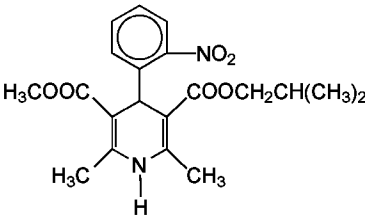
Generic name	CAS Registry Number	Molecular formula	Trade name	Structure
erythrityl tetranitrate	[7297-25-8]	C ₄ H N ₄ O ₁₂	<i>Nitrates</i> Cardilate	
isosorbide dinitrate ^a isosorbide mononitrate ^b	[87-33-2] [16051-77-7]	C ₈ H ₈ N ₂ O ₈ C ₈ H ₉ N O	Sorbitrate, Dilatrate	
nitroglycerin	[55-63-0]	C ₃ H ₅ N ₃ O ₉	Deponit, Tridil, Nitrogard, Nitro-Disc, Nitrol, Transderm-Nitro, Nitro-Dur, Nitronet, Sustarden	
pentaerythritol tetranitrate	[78-11-5]	C ₅ H ₈ N ₄ O ₁₂	Peritrate	
amlodipine besylate ^c amlodipine maleate ^d	[111470-99-6] [88150-47-4]	C ₂ H ₃₁ ClN ₂ O ₈ C ₂₄ H ₂₉ ClN ₂ O ₉	<i>Calcium channel antagonists</i>	
bepridil hydrochloride	[74764-40-2]	C ₂₄ H ₃₅ ClN ₂ O · H ₂ O O		
diltiazem hydrochloride	[33286-22-5]	C ₂₂ H ₂₇ ClN ₂ O ₄ S	Cardizem	
nicardipine hydrochloride	[54527-84-3]	C ₂ H ₃₀ ClN ₃ O	Cardene	



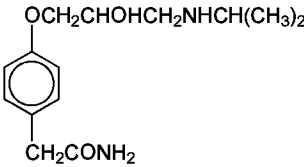
nifedipine [21829-25-4] C₁₇H₁₈N₂O Adalat, Procardia



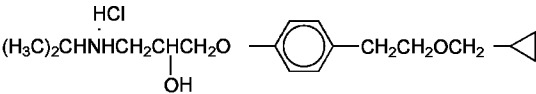
nisoldipine [63675-72-9] C₂₀H₂₄N₂O



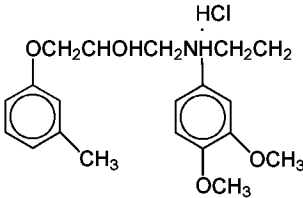
atenolol [29122-68-7] C₁₄H₂₂N₂O₃ *β -Adrenoceptor blockers*
Tenormin



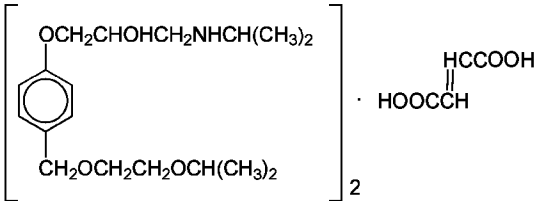
betaxolol hydrochloride [63659-19-8] C₁₈H₃₀ClNO₃



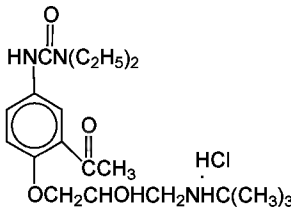
bevantolol hydrochloride [42864-78-8] C₂₀H₂₈ClNO₄ Vantol



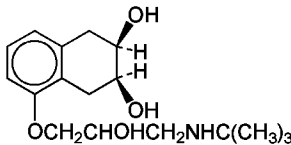
bisoprolol fumarate [104344-23-2] C₃ H₄ N₂ O₁₂ Monacor



celiprolol hydrochloride [57470-78-7] C₂₀H₃₄ClN₃O₄



nadolol [42200-33-9] C₁₇H₂₇NO₄ Corgard



^a R = NO₂.

^b R = H.
^c HA = benzene sulfonic acid.
^d HA = maleic acid.

Nitroglycerin. Nitroglycerin, originally synthesized in 1847, was introduced as a drug for the treatment of angina pectoris in 1879. It is available in sublingual tablets, ointments, and transdermal nitroglycerin delivery systems. The transdermal nitroglycerin adhesive or band-aid patches overcome problems of handling controlled dosing, ie, eliminate the peaks and valleys of plasma levels associated with conventional therapy, to achieve a prolonged duration of action. These patches consist of an outer impermeable layer, a middle and or inner drug reservoir layer, and are bordered by adhesive to attach the unit to the patient's skin. Nitro-Disc controls the rate of drug delivery by dispersing nitroglycerin in a solid polymer and uses a gel-like polymer matrix. Transderm-Nitro uses a semipermeable rate-controlling membrane between a reservoir of nitroglycerin in a viscous oil and the skin. The driving force for the nitroglycerin movement is the concentration gradient which is highest in the drug reservoir of the unit, lower through the layers of the unit, and lowest at the skin, providing a constant release of nitroglycerin into the systemic circulation. The stratum corneum of the skin is the rate determinant for the movement of the nitroglycerin. All systems are used once a day because nitroglycerin is delivered continuously for at least 24 h. The units should be applied to a hairless region of the body such as upper arm or chest and application sites should be alternated each day. The units may be worn while bathing, showering, or swimming (see CONTROLLED RELEASE TECHNOLOGY, PHARMACEUTICALS; DRUG DELIVERY SYSTEMS).

Nitroglycerin remains the drug of choice for treatment of angina pectoris. It has also been found useful for the treatment of congestive heart failure, myocardial infarction, peripheral vascular disease, such as Raynaud's disease, and mitral insufficiency, although the benefits of nitroglycerin in mitral insufficiency have been questioned.

Sublingual nitroglycerin preparations are rapidly absorbed from the oral mucosa. Peak blood levels and relief from angina occur within 1–4 min. Duration of action is 15–20 min although venous plasma nitroglycerin levels are not detectable after 10 min. Po nitroglycerin is more slowly absorbed. Maximal effects are observed in 30–60 min, and duration of action orally is 4–6 h. Nitroglycerin ointment is also slowly absorbed but its duration of action is 4–8 h. Site and area of application of the ointment appear to affect the plasma levels achieved. Using transdermal nitroglycerin systems, detectable blood levels are noted in about one hour and peak levels are noted at 4–8 h which are maintained for 24 h. Once nitroglycerin is absorbed, it is bound to plasma protein. Nitroglycerin has a large volume of distribution suggesting it is widely distributed in the body. Nitroglycerin is rapidly metabolized in the liver and other organs by glutathione organic nitrate reductase and in the blood of some species. The drug is excreted in the urine as the 1,2- and 1,3-glycerol dinitrates and some glycerol mononitrates which are pharmacologically inactive.

It was originally thought that po nitroglycerin therapy would be inadequate because absorption into portal blood, which passes directly into the liver, would allow hepatic denitration to occur on first-pass, clearing the blood of most of the drug before it reached the systemic circulation. However, glutathione organic nitrate reductase becomes saturated, slowing inactivation and allowing therapeutic nitroglycerin levels to be achieved. Drugs that increase or decrease liver microsomal enzymes may affect nitroglycerin metabolism, eg, phenobarbital [50-06-6], C₁₂H₁₂N₂O₃, (increase) and alcohol (decrease).

The principal side effects of nitroglycerin therapy are headache, nausea, flushing, dizziness, and weakness. Syncope and tachycardia can result from postural hypotension produced by nitroglycerin. The tachycardia can be attenuated by co-administration of β-adrenoceptor blocking agents. Methemoglobinemia following high doses can also occur because of oxidation of hemoglobin by nitrate ions. Whereas drug rashes resulting from ingestion of nitroglycerin are rare, there have been reports of contact dermatitis upon use of nitroglycerin ointment.

Decreased sensitivity or tolerance to the vascular effects of nitroglycerin following prolonged exposure to high doses of the drug have been reported (61). Dependence on nitrate has been observed in munitions workers exposed to glyceryl trinitrate [55-63-0], and prompt withdrawal of nitrate therapy in patients having coronary insufficiency has resulted in worsening of symptoms. Thus a gradual reduction from chronic high doses of nitroglycerin is recommended.

Isosorbide. Isosorbide dinitrate is a derivative of 1,4:3,6-dianhydro-D-glucitol [652-67-5], C₈H₁₀O₄. It is available in sublingual, chewable, regular, or time-release tablets. The drug has also been used iv. The sublingual and chewable tablets are used just prior to anginal-provoking situations (exertion) because of their short duration of action (3–5 min). The regular tablet has a duration of action of up to 3 h, and the time-release tablet up to 8 h (99).

Isosorbide is rapidly absorbed and undergoes rapid first-pass metabolism by the liver. The bioavailability of the sublingual and chewable tablets is 59% and 22%, respectively, for the regular tablet. Isosorbide is metabolized to isosorbide-2-mononitrate and isosorbide-5-mononitrate, both of which have pharmacologic activity. The elimination half-lives of sublingual and po isosorbide dinitrate are 1 and 4 h, respectively. Those of the 2- and 5-mononitrate metabolites are 1.5–3.1 h and 4–5.6 h, respectively. The two metabolites prolong the elimination half-life of the dinitrate. Adverse effects with isosorbide are similar to those described for nitroglycerin (99).

Erythrityl. Erythrityl tetranitrate is a racemic mixture of 1,2,3,4-butanetetrol tetranitrate. It is slightly less effective than nitroglycerin in reducing anginal pain but has a more prolonged duration of action. The tablet can be used sublingually or swallowed. The peak effect of swallowed doses is less but of longer duration (99).

Erythrityl is readily absorbed from the GI tract. It undergoes extensive first-pass metabolism in the liver by glutathione organic nitrate reductase. Time to onset of effect is 5–10 min by sublingual administration and 20–30 min when swallowed. The duration of effects for the two routes are up to 3 and 6 h, respectively. Adverse effects are similar to those described for nitroglycerin (99).

Pentaerythritol. Pentaerythritol tetranitrate, the tetranitrate derivative of 2,2-bis(hydroxymethyl)-1-3-propanediol [115-77-5], C₅H₁₂O₄, is available in both regular and sustained release tablet preparations. Its efficacy and pharmacokinetic and toxic properties are similar to those described for erythrityl tetranitrate (99).

Calcium Antagonist Therapy in Angina

Calcium antagonists (Table 3) alter the availability of calcium by affecting the entry of this ion into its receptor site(s). Compounds, such as verapamil (see Table 1), nifedipine, and diltiazem, were utilized for a long time for the treatment of angina and certain peripheral vascular diseases in Europe and Asia before their introduction into the United States. Calcium antagonists are used mainly in the treatment of various types of angina, hypertension, and certain arrhythmias but may have potential therapeutic applications in heart failure, acute myocardial infarction, cardioprotection, cardiomyopathy, cerebral vasospasm, and other vasospastic syndromes as well.

Calcium plays a vital role in excitation–contraction coupling, and failure to maintain intracellular calcium homeostasis results in cell death. The availability of the calcium antagonists also provides a powerful tool for basic studies of excitation–contraction coupling, stimulus–excretion coupling, and other specific physiological functions.

Calcium and Vascular Smooth Muscle Contraction. Calcium acts on a number of sites associated with the control of the cytoplasmic calcium concentration. Vascular smooth muscle contraction can be initiated by the opening of the slow calcium channel allowing influx of extracellular calcium through the sarcolemmal membrane into the cytoplasmic compartment. The intracellular calcium concentration increases to 1 × 10^{–5} M, a threshold concentration necessary to initiate contraction.

In the presence of calcium, the primary contractile protein, myosin, is phosphorylated by the myosin light-chain kinase initiating the subsequent actin-activation of the myosin adenosine triphosphate activity and resulting in muscle contraction. Removal of calcium inactivates the kinase and allows the myosin light chain to dephosphorylate myosin which results in muscle relaxation. Therefore the general biochemical mechanism for the muscle contractile process is dependent on the availability of a sufficient intracellular calcium concentration.

The calcium antagonists interfere with the entry of calcium through the membrane slow calcium channel and therefore prevent intracellular calcium

from reaching the critical concentration necessary to initiate contraction. However, these drugs may be acting through other mechanisms to prevent the elevation of the free calcium ion concentration in the cell.

The calcium antagonists produce beneficial effects in angina by either reducing coronary artery spasm, slowing heart rate, or decreasing contractile force. These effects increase oxygen supply or decrease myocardial oxygen consumption. The clinical effects are increased duration of exercise, reduction in anginal episodes, or may be a reduction in the amount of nitrate therapy consumed to reduce the anginal episode.

The cardiac effects of the calcium antagonists, ie, slowed rate (negative chronotropy) and decreased contractile force (negative inotropy), are prominent in isolated cardiac preparations. However, in the intact circulation, these effects may be masked by reflex compensatory adjustments to the hypotension that these agents produce. The negative inotropic activity of the calcium antagonists may be a problem in patients having heart failure, where contractility is already depressed, or in patients on concomitant β -adrenoceptor blockers where reflex compensatory mechanisms are reduced.

The side effects or toxic effects that the calcium antagonists have in common are hypotension, facial flushing, headache, dizziness, weakness, sedation, skin rash, edema, constipation, and abdominal discomfort (nausea, vomiting, and epigastric pressure).

Verapamil. Verapamil hydrochloride is a phenylalkylamine and is considered the prototype of the Class I calcium channel blockers. Verapamil is also a potent inhibitor of coronary artery spasm and is useful in Prinzmetal's angina and in unstable angina at rest. Verapamil produces negative chronotropic and inotropic effects. These two actions reduce myocardial oxygen consumption and probably account for the effectiveness of verapamil in chronic stable effort angina (98,99). Moreover, verapamil is an effective antihypertensive agent.

Diltiazem. Diltiazem hydrochloride, a **benzothiazepine** derivative, is considered the prototype of the Class III calcium channel blockers. The (±)-cis form of the compound is the pharmacologically active isomer. Diltiazem dilates all vascular smooth muscle equally, ie, it lacks vascular selectivity. It has potent coronary artery vasodilator properties and relieves the vasospasm of Prinzmetal's or variant angina. Its efficacy in exertional angina probably results from the ability to reduce myocardial oxygen consumption by reducing heart rate and peripheral resistance (reduce the afterload of the heart). Diltiazem is also an effective antihypertensive agent, and in addition to a cardiac negative chronotropic effect it has a slight negative inotropic effect. The electrophysiological effects include prolongations of the P–R interval, AV conduction time, and the A–H interval (1,2,98,99).

The absorption of diltiazem from the GI tract after po dosing is nearly complete. It undergoes extensive first-pass metabolism in the liver and only 40% of the po dose is bioavailable. About 70–80% of the drug is bound to plasma protein. The onset of action is about 15 min and the peak effect occurs at 30 min. Diltiazem is metabolized by deacetylation, and *N*- and *O*-demethylation. The principal metabolite, desacetyldiltiazem has 25–50% of the pharmacological activity and 10–20% of the plasma levels of the parent compound. About 30–35% of the drug is excreted by the kidneys as metabolites and 2–4% as unchanged drug. Almost 60% is excreted in the feces as metabolites. The elimination half-life of diltiazem is 3–4.5 h. Elimination half-life and plasma levels are increased in patients having liver disease (1,98,99).

The side effects of diltiazem therapy are less than those of verapamil or nifedipine therapy. Side effects occur in about 4% of the patients (1,98,99).

Nifedipine. Nifedipine is a dihydropyridine and is considered the prototype of the Class II calcium channel antagonists. The dihydropyridines are photolabile compounds and rapidly degrade when exposed to ultraviolet or visible light. At therapeutic concentration, nifedipine dilates vascular smooth muscle without compromising myocardial or skeletal muscle function (tissue selective). Nifedipine has little effect on cardiac muscle contractility in patients, but in isolated cardiac tissue preparations, nifedipine has more potent negative inotropic effects than verapamil. Nifedipine shortens the P–R interval and at high doses increases conduction time. No effect on A–H or H–V interval has been noted, nor does it have a tendency to produce AV block. Nifedipine is indicated in vasospastic angina by relaxing coronary artery spasm and in chronic stable angina by reducing oxygen consumption through reduction of afterload (peripheral vasodilation) (1,98,99).

Po administered nifedipine is almost completely absorbed. The onset of action is 20 min and peak effects occur at 1–2 h. The principal route of elimination is through hepatic metabolism by oxidation to hydroxycarboxylic acid and the corresponding lactone. These metabolites are pharmacologically inactive. Almost 70–80% of drug is eliminated in the urine during the first 24 h. About 15% is excreted in the feces. The elimination half-life of nifedipine is about 1–2.5 h (1,98,99). Frequency of occurrence of side effects in patients is about 17% with about 5% requiring discontinuation of therapy (1,98,99).

Nicardipine. Nicardipine hydrochloride is a dihydropyridine that is less photolabile than others of the Class II calcium channel blockers. It is tissue selective, producing relaxation of coronary vasculature at dose levels that produce little or no negative inotropic effects. In isolated cardiac preparations it produces a moderate negative inotropic effect and prolongs AV conduction time. Nicardipine has been shown to increase exercise tolerance, and reduce nitroglycerin consumption and the frequency of anginal attacks. It is indicated for the management of patients with chronic stable angina (1,2,98,99).

Nicardipine is almost completely absorbed after po administration. Administration of food decreases absorption. It undergoes extensive first-pass metabolism in the liver. Systemic availability is dose-dependent because of saturation of hepatic metabolic pathways. A 30 mg dose is ~35% bioavailable. Nicardipine is highly protein bound (>95%). Peak plasma concentrations are achieved in 0.5–2.0 h. The principal path of elimination is by hepatic metabolism by hydrolysis and oxidation. The metabolites are relatively inactive and exert no pharmacological activity. The elimination half-life is 8.6 h. About 60% of the dose is excreted in the urine as metabolites (<1% as intact drug) and 35% as metabolites in the feces (1,2,98,99).

Other Calcium Antagonists. Nisoldipine is a lipophilic, light-sensitive, vascular-selective dihydropyridine analogue. Dog experiments have shown that this compound effectively increased coronary blood flow and cardiac output, and decreased total peripheral resistance and systemic blood pressure. It produces a reflex tachycardia that is blocked by propranolol. Po doses significantly prolonged exercise duration and time to onset of angina in patients, by 20% (100). The antianginal effects are similar to those of nifedipine (101–103). Nisoldipine may be beneficial in hypertension (104) but not in congestive heart failure (105).

Amlodipine besylate or maleate is a lipophilic dihydropyridine analogue that is moderately light-sensitive. The compound is potent, long-acting, and selective for vascular smooth muscle. It is being studied for the treatment of angina. Unlike nifedipine, amlodipine has a very long elimination time, half-life of >33 h after iv dosing, suggesting that the drug may be given once a day. The bioavailability with po doses is 52–88% (106).

Bepridil hydrochloride, a Class VI calcium antagonist that is equiselective for heart and vascular smooth muscle, was introduced in France as an antianginal agent. It has the electrophysiological properties of Class I, ie, inhibits the fast Na channel, and Class IV antiarrhythmic agents, ie, inhibits the slow calcium channel. Clinical trials in the United States for evaluation of the antiarrhythmic effects have been discontinued because of a number of deaths in patients receiving the drug. The drug is effective in angina, reducing both the frequency of attacks and prolonging exercise time. Efficacy in angina may result from a bradycardic effect, coronary and peripheral vasodilatation, and cardiodepressant effect. Its electrophysiological effects include prolongation of the effective refractory periods of AV node, atrial and ventricular muscle, slowing of sinus rate, and prolonged QT interval in the ECG (107).

Absorption after po dosing is fairly complete. It undergoes extensive first-pass metabolism in the liver and is 60% bioavailable. It is extensively bound (99%) to α_1 -acid glycoproteins. Bepridil is almost completely metabolized in the liver. Seventeen metabolites have been identified but only the 4-hydroxy-*N*-phenyl-bepridil has some pharmacological activity. The elimination half-life is 33–42 h (107).

β-Adrenoceptor Blocker Therapy in Angina

The β -adrenoceptor blockers are effective antianginal agents because they reduce myocardial oxygen consumption and improve myocardial perfusion by several mechanisms. A decrease in heart rate increases diastolic filling time which allows for increased coronary perfusion. By decreasing blood pressure and myocardial contractility the work load of the heart and ventricular wall tension are reduced, thereby decreasing myocardial oxygen demand. The β -adrenoceptor blockers improve exercise tolerance and reduce chest pain in patients having stable exertional angina. Some of the β -adrenoceptor blockers have cardioprotective properties in patients post-MI, reducing the risk of sudden death. These agents are also useful for attenuating the reflex positive inotropic and chronotropic (tachycardia) effects in patients on nitroglycerin therapy, and in reducing the amount of nitroglycerin consumed (98,99).

Propranolol. Propranolol (Table 1), a Class II antiarrhythmic agent, is useful in the management of hypertrophic subaortic stenosis, especially for the treatment of exertional or other stress-induced angina by improving blood flow. The drug can increase exercise tolerance in patients suffering from angina. Propranolol has been shown to have cardioprotective action in post-MI patients (37–39,98,99,108).

Metoprolol. Metoprolol tartrate (Table 1), also a Class II antiarrhythmic agent, is a lipophilic, cardioselective β_1 -adrenoceptor blocking agent

having no ISA. The selectivity for β_1 -adrenoceptors may be lost at high concentrations of the drug. Metoprolol has been shown to have cardioprotective effects in post-MI patients (37–39,98,99,108).

The absorption of metoprolol after po dosing is rapid and complete. The drug undergoes extensive first-pass metabolism in the liver and only 50% of the po dose is bioavailable. About 12% of the plasma concentration is bound to albumin. The elimination half-life is 3–7 h and less than 5% of the po dose is excreted unchanged in the urine. The excretion of the drug does not appear to be altered in patients having renal disease (98,99,108).

The adverse effects noted with metoprolol result from the β -adrenoceptor blocking actions and are similar to those noted for propranolol (98,99,108).

Nadolol. Nadolol (Table 3) is a hydrophilic, nonselective β -adrenoceptor blocking agent having no ISA and no membrane-stabilizing activity. It is useful for the treatment of hypertension and chronic stable exertional angina (98,99,108).

Absorption of nadolol after po dosing is variable, averaging about 30%. The presence of food does not affect absorption. There is no hepatic first-pass metabolism and peak plasma concentrations are achieved in 3–4 h after po doses. About 30% of the plasma concentration is protein bound. The elimination half-life of nadolol is 20–24 h, allowing once a day dosing. The drug is excreted unchanged by the kidneys and its excretion is delayed in patients having renal failure (98,99,108).

Atenolol. Atenolol is a lipophilic, cardioselective β -adrenoceptor blocking agent having no ISA. The cardioselectivity decreases with increasing doses or concentrations of the drug. Atenolol is indicated for the long-term management of patients having angina pectoris as a result of coronary atherosclerosis because the β -adrenoceptor blocking actions can reduce catecholamine-induced increase in blood pressure, heart rate, and myocardial contractility, together with myocardial oxygen consumption. Atenolol has also been shown to reduce the incidence of sudden death in post-MI patients (98,99,108).

After po doses, atenolol is rapidly but incompletely absorbed (~50%) from the GI tract, and 50% is excreted unchanged in the feces. Six to 16% of the plasma concentration is bound to protein. Atenolol undergoes little first-pass metabolism. Peak plasma concentrations occur in 2–4 h after po doses. The elimination half-life of atenolol is 6–7 h. Excretion of absorbed drug is mainly by the kidneys and elimination can be impaired in patients having renal failure. The adverse effects of atenolol are similar to those seen for propranolol therapy (98,99,108).

Other β -Adrenoceptor Blocking Agents. Carteolol hydrochloride (Table 1) is also a Class II antiarrhythmic agent. In three separate studies in patients having angina pectoris, carteolol was considered effective as evidenced by a reduction in the frequency and severity of anginal episodes, reduction in the amount of nitroglycerin consumed, improvement of ECG parameters, or an increase in the duration of treadmill exercise (42).

Betaxolol hydrochloride is a lipophilic, cardioselective β -adrenoceptor blocker having no ISA and little membrane-stabilizing activity. The drug is as equieffective and equipotent as atenolol. It is well absorbed from the GI tract, but does not undergo extensive first-pass metabolism in the liver. Its elimination half-life is 15–20 h. It is metabolized in the liver (~84%) to two principal inactive metabolites and one minor active metabolite. About 16% of the drug is excreted unchanged urine. Excretion of the drug is unchanged in patients having renal or liver impairment (43).

Bisoprolol fumarate is a long-acting, cardioselective β -adrenoceptor blocker, and is the most potent cardioselective β -adrenoceptor blocker available. Bisoprolol has no ISA. At high concentrations it has membrane-stabilizing activity. The drug has a "balanced clearance", ie, half is excreted by the kidneys and half is eliminated by the liver and its excretion is not affected by functional impairment of either organ. It is approved in Europe for hypertension and is being studied in angina (43).

Celiprolol hydrochloride is a hydrophilic, long-acting, cardioselective β -adrenoceptor blocker. In addition to ISA, the compound has weak α_2 -adrenoceptor blocking action at high concentrations. No membrane-stabilizing activity has been noted with celiprolol. Food interferes with the absorption of celiprolol. Bioavailability is about 30 and 74% in fed and fasted subjects, respectively. The drug is not metabolized by the liver but is excreted through the bile into the feces and via the kidneys. Peak drug levels occur in 2–3 h and its elimination half-life is about 5 h. The drug is being developed as an antihypertensive and antianginal agent. It has shown efficacy in treating stable angina (43).

Bevantolol hydrochloride is a moderately lipophilic, long-acting, cardioselective β -adrenoceptor blocker. It has no ISA but has membrane-stabilizing activity. The drug is in use in Europe for the treatment of hypertension and angina. It is rapidly absorbed from the GI tract. Peak plasma levels occur in 1–2 h. It is metabolized extensively in the liver to a metabolite that has some ISA. It is excreted by the liver and the kidneys and excretion is delayed in patients having kidney failure.

AGENTS USED IN THE TREATMENT OF CONGESTIVE HEART FAILURE

Congestive heart failure (CHF) is an ever present, growing health problem in the United States. Over 2 million people have been diagnosed as having CHF, and more are expected to be diagnosed as the mean age of the population increases (109). CHF presents a special problem because of its high annual mortality rate of 20–50% (110). This high mortality rate is largely the lack of a pharmacologic agent that can improve the prognosis for cure above and beyond symptomatic relief. As of this writing there is a great deal of research centered on improved pharmacotherapeutic agents for the treatment of CHF.

Physiology and Biochemistry of Congestive Heart Failure

The heart, a four-chambered muscular pump has as its primary purpose the propelling of blood throughout the cardiovascular system. The left ventricle is the principal pumping chamber and is therefore the largest of the four chambers in terms of muscle mass. The efficiency of the heart as a pump can be assessed by measuring cardiac output, left ventricular pressure, and the amount of work required to accomplish any required amount of pumping.

When the heart begins to fail as a pump, a number of pathophysiologic processes occur. Perhaps the easiest to perceive is simply that some of the blood within the left ventricle is not completely expelled during muscle contraction or systole. This subsequently requires more work during future systoles as additional blood returns from the pulmonary vein. A sort of congestion begins to develop as the heart cannot develop enough pumping ability to provide adequate oxygenated blood to the arterial circulation or removal of metabolic waste through the venous circulation.

There can be a number of underlying causes of CHF. The most prevalent is the lack of oxygenated blood reaching the heart muscle itself because of coronary artery disease with myocardial infarction (111). Hypertension and valvular disease can contribute to CHF as well, but to a lesser extent in terms of principal causes for the disease.

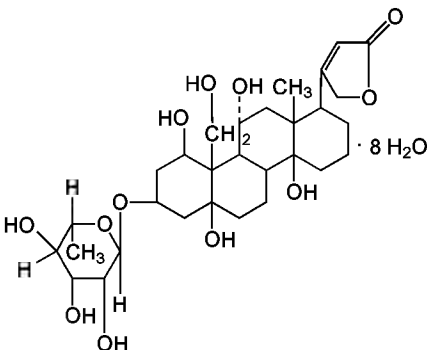
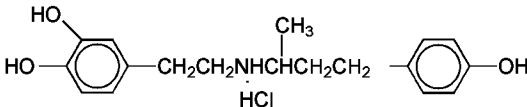
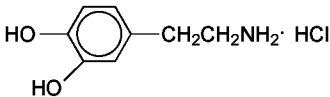
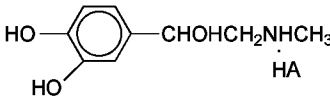
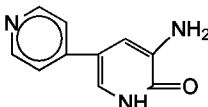
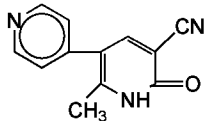
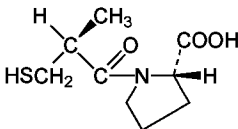
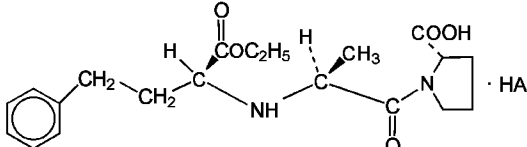
Both high energy containing adenosine triphosphate (ATP) and calcium are integral components of cardiac muscle contraction. Hydrolysis of ATP is coupled to cross-linking of the actin–myosin contractile proteins, resulting in mechanical shortening of the functional unit of cardiac muscle, the sarcomere. Calcium is involved in binding of the contractile protein troponin, but the quantity of calcium entering the myocardial cell is finely regulated, concomitantly regulating the extent of cardiac muscle contraction. Imbalance in any aspects of the chemical process of contraction can result in reduced pumping ability, and contribute to CHF.

Therapy of Congestive Heart Failure

Many of the drugs used to combat congestive heart failure are inotropic agents, some of which are shown in Table 4. Inotrope is a derivation of the Greek *ino* (fiber) and *tropikos* (changing or turning). A positive inotropic agent is therefore one that increases cardiac muscle contractility associated with CHF.

Table 4. Inotropic Agents

Generic name	CAS Registry Number	Molecular formula	Trade name	Structure

ouabain octahydrate	[630-60-4]	C ₂₉ H ₄₄ O ₁₂	<i>Glycosides</i>	
dobutamine hydrochloride	[49745-95-1]	C ₁₈ H ₂₄ ClNO	<i>Catecholamines</i> Dobutrex	
dopamine hydrochloride	[62-31-7]	C ₈ H ₁₂ ClNO ₂	Dopastat, Intropin	
epinephrine bitartrate ^a	[51-42-3]	C ₁₃ H ₁₉ NO ₉	Epitrate, Suprarenin	
amrinone	[60719-84-8]	C ₁₀ H ₉ N ₃ O	<i>Phosphodiesterase inhibitors</i> Inocor	
milrinone	[78415-72-2]	C ₁₂ H ₉ N ₃ O	Primacor	
captopril	[62571-86-2]	C ₉ H ₁₅ NO ₃ S	<i>Angioten converting enzyme inhibitors</i> Capoten	
enalapril maleate ^b	[76095-16-4]	C ₂₄ H ₃₂ N ₂ O ₉	Vasotec	

^a HA tartaric acid.
^b HA malonic acid.
^c Registry number given is for anhydrous material.

The Cardiac Glycosides. As early as the 1700s the medicinal properties of the leaves of *Digitalis purpurea* (foxglove), which was used by physicians of that time for treatment of dropsy, was described (112). The leaves of *Digitalis purpurea* yield digitoxin (Table 1); whereas *Digitalis lanata* is used for production of digoxin (Table 1) through mild alkaline hydrolysis. The seeds of *Strophanthus gratus* is used to obtain ouabain, which is a rapidly acting glycoside. Digoxin is the most commonly prescribed cardiac glycoside in the United States, because of its intermediate duration of action, various routes of administration, and ease in which serum levels can be determined (113).

The cardiac glycosides are composed of a steroid aglycone (genin) in combination with from 1 to 4 moles of a sugar, some of which are acetylated. The genins, generally considered to poison through convulsion, have some activity for use in CHF, but the sugar moiety contributes both to potency and to transport. The glycosides remain an enigma to cardiologists, however, because of the combination of extreme potency and low margin of safety.

Mechanism of Action. Digitalis has particular efficacy in the treatment of congestive heart failure because of direct inotropic effects on the heart which serve to increase the force of myocardial contraction, resulting in increased cardiac output and alleviation of the congestion. The mechanism mediating this positive inotropic effect is through direct inhibition of the enzyme Na⁺, K⁺-ATPase, which in turn promotes elevated intracellular calcium. Digitalis also has direct effects on the electrical activity of the heart, affecting the normal physiologic function of the sinoatrial node, the atrioventricular node, and the Purkinje fibers. The ramifications of the direct effect of digitalis on cardiac electrical activity is a slowing of heart rate, but can also include

digitalis-induced arrhythmias (114).

Digitalis is also beneficial in the treatment of CHF because of direct effects on the central nervous system. Efferent vagus nerve activity is promoted by digitalis administration, resulting in an indirect slowing of heart rate. Digitalis in relatively high concentrations can enhance efferent sympathetic nervous system activity, purportedly inhibit reuptake of norepinephrine, and ultimately promote arrhythmogenesis (114).

Moreover, digitalis has indirect effects on the circulation, which in normal hearts results in a small increase in arterial pressure, peripheral resistance, and cardiac output (114). The effects of digitalis on the circulation of an individual experiencing congestive heart failure are much more dramatic, however. The increased cardiac output, for example, increases renal blood flow which can relieve in part the edema of CHF associated with salt and water retention (114).

When administered orally, digoxin bioavailability ranges from 40 to 90% depending on the manufacturing process. Peak plasma levels occur within 3 h after oral administration; peak effects occur 2 h later. The drug is eliminated primarily through the kidney (114).

Ouabain, structurally related to digitalis, is a very potent analogue often used in experimental studies. In the 1980s, a number of critically controlled clinical studies were undertaken to better understand the benefits and risks of digoxin therapy (115–117). It was concluded from these studies that patients having mild CHF, ie, not severe enough to limit daily activities, did not benefit from digoxin, even though the drug remains an appropriate therapy for patients having more extensive left ventricular dysfunction (118).

Cardiac Glycoside Toxicity. Digoxin remains a drug with considerable limitations because of toxicity, among which the most dangerous are the electrophysiologic effects. The drug can slow atrial rate and atrioventricular node conduction, leading to arrhythmia (119). In fact, because almost every variety of ventricular arrhythmia has been associated with digitalis toxicity (113), the drug can complicate, not eradicate, the treatment of CHF. Importantly, antiarrhythmic agents such as lidocaine and phenytoin can suppress digoxin-induced arrhythmia. More recently high affinity antidigoxin antibodies, specifically the *Fab* fragment, have become widely available to clinicians (120). The antibodies have greatly increased the safety of prescribing digitalis.

Nondigitalis Inotropic Agents. A number of inotropic agents that are not structurally related to the cardiac glycosides have been investigated for treatment of CHF. All are somehow mechanistically related to the complex series of events involved in normal cardiac muscle contraction, and in terms of pumping ability are capable of increasing left ventricular contractility. Many of these drugs do not perform in diseased cardiac tissue in a manner similar to that observed in normal, nondiseased muscle. Many of these agents act via the β -adrenergic receptors of the sympathetic nervous system (SNS).

Catecholamines. Simplistically, the SNS is composed of nerves capable of synthesizing and releasing various catecholamines that can bind appropriate molecular receptors post-synaptically. Dependent on their synthetic structure, they have the ability to bind, and therefore stimulate various post-synaptic events through α , β , and dopaminergic receptors.

Each receptor has a specific role, often vasodilation, which serves to facilitate the ability for a failing heart to pump against a reduced systemic pressure. Side effects of catecholamines include arrhythmias and tachyphylaxis. In addition, potent vasodilators such as isoproterenol [7683-59-2], $C_{11}H_{17}NO_3$, have a dual effect, namely increased contractility through direct cardiac muscle stimulation (121). If combined with significant reductions in blood pressure, isoproterenol can produce detrimental effects through a combination of reduced venous return yet increased oxygen requirements of the rapidly contracting cardiac muscle. The orally active catecholamine pirbuterol [38677-81-5], $C_{12}H_{20}N_2O_3$, has many of these classic side effects (121). These drugs have been selectively developed to affect specific receptor subtypes through radioligand binding studies using microsomal membrane preparations from animal tissue. This rapid method of screening for selective agonists and antagonists has produced considerable quantities of chemical structures that have potential as drugs. Each results in positive, yet relatively short-term efficacy in patients having CHF (122).

Dobutamine, a positive inotrope from the sympathomimetic amine family, was introduced in the early 1980s and possesses an asymmetric carbon atom resulting in two enantiomers. The commercial product is a 50:50 racemic mixture of the optical isomers, producing a combined β -adrenergic agonist and α -adrenergic antagonist effect (123) from the (+) enantiomer. The (-) enantiomer is a potent α -adrenoceptor agonist (124). The positive inotropic activity is a result of the two enantiomers, especially as relates to functional, simultaneous effects on cardiac and vascular smooth muscle. Because of this unique combination of activity, dobutamine is superior to isoproterenol, dopamine, epinephrine, and norepinephrine, primarily because of dobutamine's lesser effect on blood pressure reduction. At doses of 2.5–15 μg (kgmin) dobutamine increases stroke volume, while reducing peripheral resistance. Even after drug infusion is stopped, the patient can continue to benefit (125). Because it is administered by infusion, the drug is not approved by the FDA for outpatient administration.

Drugs Acting on the β -Adrenoceptor. The increase in plasma norepinephrine observed in heart failure is considered to be responsible to a large part for a reduced β -adrenoceptor number in cardiac membranes (126). This down-regulation of β -adrenoceptors affects predominantly the β_1 -subtype whereas the β_2 -subtype remains normal. In 1982, experimental data from normal and failing myocardium, noting both a reduced binding capacity and post-receptor adenylyl cyclase-mediated papillary muscle contraction in the failing heart, was published (127). These changes in the β -adrenoceptor system of patients having CHF have therapeutic implications against treatment with β -antagonists.

The use of selective β -antagonists for treatment of CHF has included the β_1 -blocker metoprolol (Table 1) and results of clinical trials suggest long-term beneficial effects. Selective β_1 -antagonists have also been tested, an example of which is xamoterol [81801-12-9], $C_{11}H_{25}N_3O_5$, which is (±)-N-(2-hydroxy-3-(4-hydroxyphenoxy)propylamino)ethyl morphine-4-carboxamide. Xamoterol exhibits approximately 50% of the activity of isoproterenol, and serves to provide modest inotropic effects (128,129).

Phosphodiesterase Inhibitors. Because of the complexity of the biochemical processes involved in cardiac muscle contraction, investigators have looked at these pathways for other means of drug intervention for CHF. One of the areas of investigation involves increased cyclic adenosine monophosphate [60-92-4] (cAMP) through inhibition of phosphodiesterase [9025-82-5] (PDE). This class of compounds includes amrinone, considered beneficial for CHF because of positive inotropic and vasodilator activity. The mechanism of inotropic action involves the inhibition of PDE, which in turn inhibits the intracellular hydrolysis of cAMP (130). In cascade fashion, cAMP-catalyzed phosphorylation of sarcolemmal calcium-channels follows, activating the calcium pump (131). A series of synthetic moieties including the bipyridines, amrinone and milrinone, piroximone and enoximone, [77671-31-9], $C_{12}H_{12}N_2O_2S$, all of which have been shown to improve cardiac contractility in short-term studies, were developed (132,133). These drugs initially had a wider therapeutic index than cardiac glycosides, and did not exhibit receptor down-regulation associated with β -adrenoceptor blockers. Questions have since surfaced concerning the detrimental effects of increased contractility upon accelerated deterioration of already diseased cardiac tissue, ie, these drugs can lead to shortened patient survival (134,135). An additional detrimental side effect is arrhythmogenesis (136).

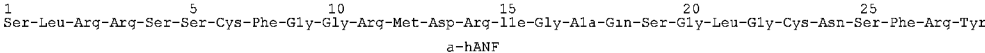
Angiotensin Converting Enzyme Inhibitors. The angiotensin converting enzyme (ACE) inhibitors represent another nonglycoside method of treating CHF. A number of these drugs are in various stages of development. The first such was introduced as captopril [62571-86-2], $C_9H_{15}NO_3S$, in the 1980s. This drug produced reductions in both preload and afterload, and although originally marketed as an antihypertensive, this profile indicated potential efficacious therapy for CHF (137,138). The effect in acute heart failure can be seen in 30–360 min, depending on the specific ACE inhibitor employed (139). Controlled clinical studies have shown the ACE inhibitors are at least equal in effectiveness to cardiac glycosides in treatment of CHF (140), and may actually elicit a positive effect on the pathophysiologic mechanism of CHF by inhibiting angiotensin II formation.

ACE inhibitors can be administered with diuretics (qv), cardiac glycosides, β -adrenoceptor blockers, and calcium channel blockers. Clinical trials indicate they are generally free from serious side effects. The effectiveness of enalapril, another ACE inhibitor, in preventing patient mortality in severe (Class IV) heart failure was investigated. In combination with conventional drugs such as vasodilators and diuretics, a 40% reduction in mortality was observed after six months of treatment using 2.5–40 mg d of enalapril (141). However, patients complain of cough, and occasionally rash and taste disturbances can occur.

Atrial Natriuretic Factor. Atrial natriuretic factor (ANF) has natriuretic, vasorelaxant, and diuretic properties (142). It was originally discovered in atrial tissue, from which extracts were made and subsequently injected systematically. The responses evoked from the atrial extracts established the heart as an endocrine organ.

A number of different types of ANF have been described, but the original molecule is a polypeptide of 28 amino acids (qv). The prepro-form is released from the atria by stretch, suggesting that increased blood volume in a poorly contracting atria compromised by CHF could be one

pathophysiologic condition in which the hormone would prove efficacious. As of this writing, this peptide has not received FDA approval. However, a number of clinical studies have been performed. For example, a single 33 μm bolus of ANF was injected into normal volunteers and patients having volume retaining disorders (143), including CHF. Patients with end-stage renal failure and CHF showed blunted hemodynamic responses to ANF, whereas the healthy control patients also exhibited greater urinary excretion of sodium.



Although the potential of ANF has not been realized as a marketed drug for treatment of CHF, the fact that a small peptide can have such profound effects on hemodynamics and renal physiology has led to considerable excitement. This enthusiasm is based in part on the advent of molecular biological techniques for ease in production of large quantities of naturally occurring peptides, as well as the ability to use these techniques for understanding how the peptide is processed beginning at the level of genomic DNA (see [PROTEIN ENGINEERING](#)).

ATHEROSCLEROSIS AND ANTIATHEROSCLEROSIS DRUGS

Formation of atherosclerotic plaques (atheromas) remains one of the central processes in cardiovascular death, including coronary heart disease. Complications from atheromas in coronary arteries include myocardial infarction and stroke. This latter is a common manifestation of cerebral vascular plaque formation. Atherosclerotic plaques begin as fatty streaks which progress to defined plaques containing cholesterol [57-88-5], C₂₇H₄ O, eventually being overlaid with connective tissue (144). The atheroma can be initiated by vascular injury, and once formed can be the site for thrombus formation and blood platelet deposition, which eventually become calcified. The existence of such formations in arterial walls can produce serious reductions in blood flow to the organs being supplied by these diseased arteries, producing local ischemia. The atheromas therefore present an especially dangerous health problem when situated in arteries supplying blood to cardiac muscle and brain.

Reduction in serum lipids can contribute significantly to prevention of atherosclerosis. In 1985 a consensus report indicating that for every 1° reduction in serum cholesterol there is a 2° reduction in adverse effects of coronary heart disease was issued (145). Recommended serum cholesterol concentration was 200 mg dL for individuals under 30 years of age, and individuals having concentration 240 mg dL and LDL-cholesterol over 160 mg dL should undertake dietary modification and possibly pharmacotherapy (146). Whereas the initial step in reducing serum cholesterol is through reduction of dietary cholesterol intake, a number of drugs are available that can affect serum lipid profile (see [FAT SUBSTITUTES](#)). The pathway to cholesterol synthesis is shown in Figure 2.

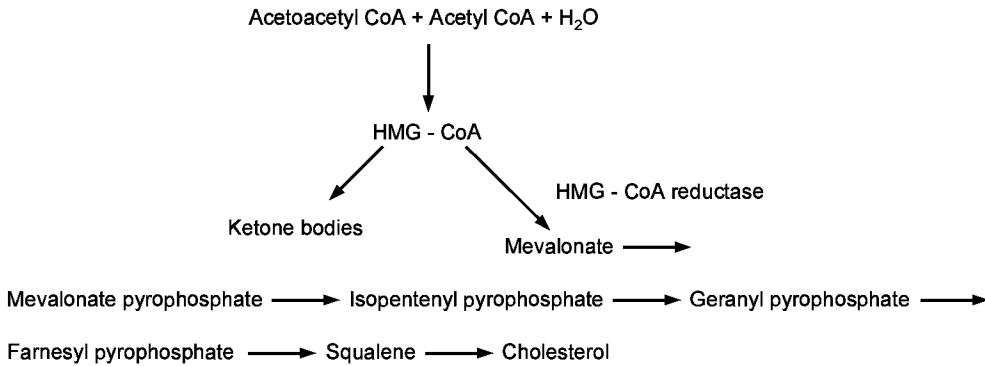
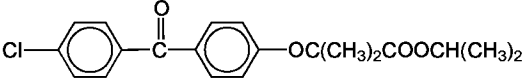
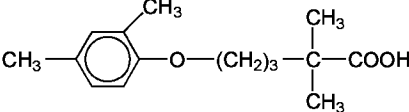
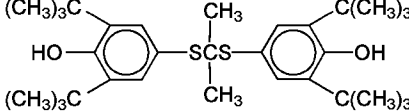


Fig. 2. Pathway of cholesterol synthesis.

The primary transporter of cholesterol in the blood is low density lipoprotein (LDL). Once transported intracellularly, cholesterol homeostasis is controlled primarily by suppressing cholesterol synthesis through inhibition of β-hydroxy-β-methyl glutarate-coenzyme A (HMG–CoA) reductase, acyl CoA–acyl transferase (ACAT), and down-regulation of LDL receptors. An important drug in the regulation of cholesterol metabolism is lovastatin, also known as mevinolin, MK-803, and Mevacor, which is an HMG–CoA reductase inhibitor (Table 5).

Table 5. Antiatherosclerosis Drugs

Generic name	CAS Registry Number	Molecular formula	Trade name	Structure
<i>HMG-CoA reductase inhibitor</i>				
lovastatinMK-803mevinolin	[75330-75-5]	C ₂₄ H ₃ O ₅	Mevacor	
<i>Lipid lowering drugs</i>				
bezafibrate	[41859-67-0]	C ₁₉ H ₂₀ ClNO		
clofibrate	[637-07-0]	C ₁₂ H ₁₅ ClO ₃	Atromid-S	
fenofibrate	[49562-28-9]	C ₂₀ H ₂₁ ClO ₄		

			
gemfibrozil	[25812-30-0]	C ₁₅ H ₂₂ O ₃	
			
probucol	[23288-49-5]	C ₃₁ H ₄₈ O ₂ S ₂	Antioxidants: Cholesterol lowering agents Lorelco
			

A fermentation product of the fungus *Aspergillus terreus*, lovastatin was originally described as a cholesterol-lowering agent in 1980 (147). Through inhibition of the rate-limiting enzyme of cholesterol synthesis, HMG–CoA reductase, the drug interferes with mevalonic acid [150-97-0], C₅H₁₂O₄, synthesis. Lovastatin is actually a pro-drug, which is eventually hydrolyzed in the liver to its active, β-hydroxylated form (148). Oral lovastatin is prescribed in a once a day regimen of 20–80 mg d. It exhibits significant plasma protein binding, and only about 5% of the oral dose reaches the general circulation.

In the first clinical studies with lovastatin, pre-drug serum cholesterol values of 150–300 mg dL were shown to be decreased as much as 25% with a dosage of 15 mg twice daily for just over a week (149). Whereas the drug shows few adverse side effects, gastrointestinal disturbances, including diarrhea and abdominal pain, are the most common.

Bile Acid Sequestrants. The bile acid binding resins, colestipol [26658-42-4] and cholestyramine, are also effective in controlling serum cholesterol levels (150). Cholestyramine, a polymer having mol wt > 10⁶, is an anion-exchange resin. It is not absorbed in the gastrointestinal tract, is not affected by digestive enzymes, and is taken orally after being suspended in water (151).

Colestipol, also an anion-exchange copolymer, is composed of diethylenetriamine [111-40-0], C₄H₁₃N₃, and 1-chloro-2,3-epoxypropane [106-89-8] C₃H₅ClO. Its metabolism and formulation is quite similar to cholestyramine. Because bile acids are synthesized from cholesterol, bile acid sequestrants such as cholestyramine and colestipol, through binding bile acids in the intestine, can affect cholesterol metabolism. The drug–bile acid complex is eventually excreted in the feces, effectively reducing the total cholesterol pool in the body. In fact, these drugs have been shown to be effective in decreasing both LDL-cholesterol and total serum cholesterol. Use, however, is limited to patients having hypercholesterolemia not associated with hypertriglyceridemia, also known as Type II hyperlipoproteinemia. The drug-induced reduction in cholesterol can be dramatic; as much as 50% reduction can be observed over long-term therapy (152). Thus control of serum cholesterol can contribute to the antiatherosclerotic attributes of this class of drug.

Because colestipol and cholestyramine are not absorbed, but simply pass through the body by the GI tract, few severe side effects occur. Patients often complain of distaste and constipation, however. More severe side effects such as GI bleeding are relatively uncommon (151).

Fibric Acid Derivatives. Fibric acid derivatives have been used since the 1960s for control of blood lipid levels. The four most well-known compounds in this class are fenofibrate, gemfibrozil, clofibrate, and bezafibrate, shown in Table 5. Fenofibrate has been the most popular fibric acid derivative in Europe, and has more recently been investigated extensively in clinical trials in the United States (153). Bezafibrate is structurally related to clofibrate, and has recently been reviewed by Western European and Australian clinical trials (154).

Clofibrate, shown to be an effective lipid lowering drug in the early 1960s, is the ethyl ester of *p*-chlorophenoxy isobutyric acid. Gemfibrozil is a structural congener of clofibrate.

The mechanism of action of the fibrates in controlling plasma lipids appears to be primarily through mediation of lipoprotein lipase activity. In addition, gemfibrozil stimulates apolipoprotein AI synthesis (155), presumably leading to increased high density lipoprotein (HDL) particles. In fact, the mechanistic effects of the fibrates in lowering serum cholesterol are complex, from indirect regulation of lipoprotein synthesis, to regulation of key enzymes and receptors involved in lipid metabolism. These drugs are well absorbed after oral administration. For example, in single-dose studies of 400 mg d, almost complete absorption of bezafibrate was observed, followed by virtually 100% excretion within 48 h (156).

Adverse side effects of the fibric acid derivatives are similar to those of the bile acid sequestrants. Patients complain of GI effects, including nausea and vomiting. Generally speaking, these drugs are most often prescribed for Type IIa and IIb hyperlipidemia, and are effective in reducing plasma triglycerides and very low density lipoprotein (VLDL) cholesterol. Based on the increasing evidence that reduced cholesterol can contribute to prevention of atherosclerosis, these drugs can lead to reduction in cardiovascular disease.

Nicotinic acid [59-67-6], C₆H₅NO₂, has been known as a hypolipemic since the mid-1950s. Dosages of 2–8 g daily reduce serum triglycerides primarily through decreasing the production of very low density lipoprotein. Side effects include pruritus and gastrointestinal disturbances. This drug is suggested for use in patients not responding to dietary interventions for lowering blood lipids.

Other Cardiovascular Agents Effecting Atherosclerosis. A large amount of clinical data is available concerning serum lipid profiles in patients subjected to drug therapy for other cardiovascular diseases. Atheroma, for example, may be the underying cause of hypertension and myocardial infarction. There are on the order of 1.5 million heart attacks per year in the United States (155).

β-Adrenoceptor Antagonists or Blockers. Although having no overt effects on total plasma cholesterol, β-adrenoceptor blockers (Table 1) are somewhat effective in reducing acute cardiac insult resulting from atherosclerosis. By decreasing myocardial oxygen requirements, β-blockers can effectively decrease death from myocardial infarction, which is contributed to largely by atherosclerotic coronary artery disease. Because β-blockers can inhibit catecholamine-receptor agonist responses, including atheroma development, these drugs can slow the formation of plaques that could prove potentially dangerous (157). Mechanistically, this may occur by reducing endothelial cell permeability to lipoproteins, inhibiting ACAT, or simply reducing blood flow and heart rate (158).

Calcium Channel Blockers. Because accumulation of calcium is one of the facets of the more involved process leading to atherosclerosis, it would follow that the antihypertensive calcium channel blockers might be effective in preventing atheroma. Both verapamil (Table 1) and nifedipine (Table 3) have been shown to stimulate the low density lipoprotein (LDL) receptor (159). This specific receptor-mediated pathway could theoretically improve lipid metabolism in the arterial wall, and thereby prove antiatherogenic. These effects have been proven in animals.

Probucol. Probucol is an antioxidant that is effective in lowering LDL cholesterol. Whereas probucol was known to lower cholesterol after relatively simple clinical trials (160), its mechanism of action as an antioxidant in the treatment of atherosclerosis is quite novel. Probucol has been shown to have the ability to produce regression of atherosclerotic lesions in animal models (161). Probucol therefore represents a novel class of pharmaceutical agent for the treatment of atherosclerosis. This effect occurs mechanistically, in part, by preventing oxidation of LDL, a necessary step in foam cell formation. This antioxidant activity has been shown in laboratory experiments and its activity in lowering LDL cholesterol in human studies is well documented (162).

ANTIHYPERTENSIVE AGENTS

Hypertension is one of the two principal risk factors of many cardiovascular diseases, such as coronary heart disease (CHD), stroke, and CHF. Individuals are considered hypertensive if their systolic arterial blood pressure is over 140 mm Hg (18.7 Pa) or their diastolic arterial blood pressure is over 90 mm Hg (12 Pa). Over 60 million people, or one-third of the adult population in the United States are estimated to be hypertensive (163). About 90% of these patients are classified as primary or essential hypertensive because the etiology of their hypertension is unknown. It is generally agreed that there is a very strong genetic or hereditary component to this disease.

Arterial blood pressure at any given time is determined by the balance of the vasopressor and vasodepressor systems operating in various organs and tissues of the body. Some of the principal vasopressor systems identified are the adrenergic or sympathetic nervous system; the renin–angiotensin–aldosterone system (164); the thromboxane and the prostaglandin $F_2\alpha$ systems (165,166); vasopressor peptides; endothelin (167), endothelium-derived contracting factors (EDCF) (168,169); the kidney blood volume regulation system (170,171); and the vasopressin system (172). Some of the primary vasodepressor systems are the cholinergic or parasympathetic nervous system, the kallikrein–kinin system, prostaglandin E_2 and prostacyclin (epoprostenol, PGI_2) (166,173,174), atrial natriuretic factor (ANF) (175), endothelium-derived relaxing factors (EDRF) (168,169), and the renal neutral-lipids system. The central nervous system (CNS) can exert either a vasopressor or vasodepressor influence, depending on the level of homeostasis. Overactivity of the vasopressor systems with normal vasodepressor systems causes hypertension. On the other hand, normal vasopressor systems having underactivity of deficiency of opposing vasodepressor systems theoretically can also lead to hypertension.

It is well accepted that hypertension is a multifactorial disease. Only about 10% of the hypertensive patients have secondary hypertension for which causes, ie, partial coarctation of the renal artery, pheochromacytoma, aldosteronism, hormonal imbalances, etc, are known. The hallmark of hypertension is an abnormally elevated total peripheral resistance. In most patients hypertension produces no serious symptoms particularly in the early phase of the disease. This is why hypertension is called a silent killer. However, prolonged suffering of high arterial blood pressure leads to end organ damage, causing stroke, myocardial infarction, and heart failure, etc. Adequate treatment of hypertension has been proven to decrease the incidence of cardiovascular morbidity and mortality and therefore prolong life (176–183).

Treatment of Hypertension

Treatment of essential or primary hypertension emphasizes not only the lowering of the elevated blood pressure, but also individualized therapy for each patient, providing each patient with minimized unnecessary side effects. The patient's cardiovascular morbidity and mortality should be decreased and end organ damage reversed or reduced (184,185).

Of the patients diagnosed to have essential hypertension, about 70% have mild hypertension where the diastolic blood pressure is from 90 to 104 mm Hg (12–13.9 Pa), 20% have moderate hypertension, ie, 105–114 mm Hg (14–15.2 Pa), and 10% have severe hypertension, >115 mm Hg (15.3 Pa). Once sustained hypertension is determined, nonpharmacological treatment as initial therapy is generally recommended for six months only for patients having diastolic blood pressure less than 100 mm Hg (13.3 Pa) when no evidence of target end organ damage is detected. Nonpharmacological measures include reductions in salt intake, weight, and alcohol consumption, and increases in potassium intake and physical exercise. Drug therapy is generally life-long for most hypertensive patients.

The Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure detailed a recommendation in 1988 (JNC-IV) that emphasized an individualized or patient-oriented (demographic) approach. Factors affecting each patient should be taken into consideration in choosing an antihypertensive drug. The first drug should be either an angiotensin converting enzyme (ACE) inhibitor, a β -adrenoceptor blocker, a calcium channel blocker, or a diuretic. One drug can normalize the blood pressure of about 50–60% of the hypertensive patients and the combination of two complementary drugs normalizes that of over 80% patients. White, young, hyperdynamic, hypertensive patients start with an ACE inhibitor or a β -adrenoceptor blocker; older patients respond well to a calcium channel blocker or a diuretic as do black hypertensive patients; patients having left ventricular hypertrophy respond well to an ACE inhibitor, a calcium channel blocker, or an α_2 -adrenoceptor agonist; and patients having concomitant CHF, stroke, diabetes, or hypercholesterolemia can start with an ACE inhibitor.

Patients having high plasma renin activity (PRA) (>8 ng (mLh)) respond best to an ACE inhibitor or a β -adrenoceptor blocker; those having low PRA (<1 ng (mLh)) usually elderly and black, respond best to a calcium channel blocker or a diuretic (184). β -Adrenoceptor blockers should not be used in patients who have diabetes, asthma, bradycardia, or peripheral vascular diseases. The thiazide-type diuretics (qv) should be used with caution in patients having diabetes. Likewise, β -adrenoceptor blockers should not be combined with verapamil or diltiazem because these drugs slow the atrioventricular nodal conduction in the heart. Calcium channel blockers are preferred in patients having coronary insufficiency diseases because of the cardioprotective effects of these drugs.

For patients having a moderate level of PRA, an ACE inhibitor is often tried first. The alternative is a calcium channel blocker. If neither one can control the elevated blood pressure, a combination of the two is used to block both vasoconstrictor mechanisms. The alternative combination is an ACE inhibitor and a diuretic (184,186). Other classes of antihypertensive agents are used if proven to be superior to these first-line agents, or added to the first-line drugs to increase efficacy or to decrease side effects. The goal is to give each patient the fewest number of drugs, using the smallest effective amounts having the lowest frequency of dosing and minimum side effects (184,187). Ie, optimal therapy should reduce all risk factors of coronary heart diseases, reverse the hemodynamic abnormalities present by preserving cardiac output and tissue perfusion, and lower total peripheral resistance. The challenge is to choose the best antihypertensive drug for concomitant existing diseases while maintaining a good quality of life (188–199).

The various antihypertensive agents classified according to mechanism are as follows:

Agents Affecting the Renin-Angiotensin System

Angiotensin converting enzyme inhibitors

captopril

enalapril

lisinopril

perindopril, ramipril, spirapril, quinapril, alacepril, delapril, ceranapril, zofenopril, fosinopril, benazepril, libenzapril

Angiotensin II receptor antagonists

DuP 753, DuP 532

EXP-9993, EXP-3174

L-158,809

Renin inhibitors

Enalkiren (A-64662)

CGP 38 560 A

CP 71362

KRI-1230, U-71039, ES6864, PD-134672

Agents Affecting the Adrenergic Nervous System

Ganglionic blockers

chlorisondamine

trimethaphan

hexamethonium

Neuronal blockers

guanethidine

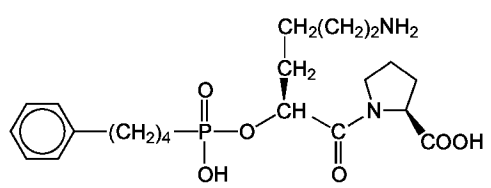
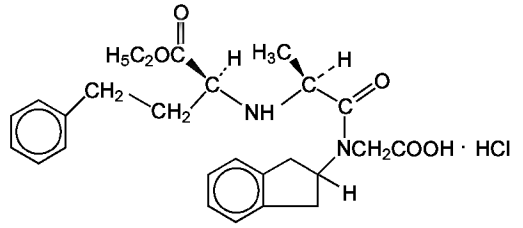
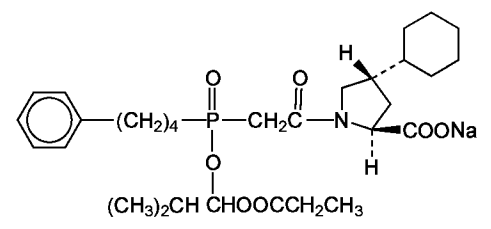
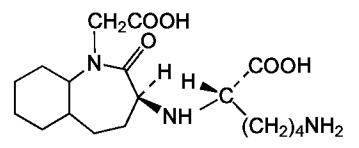
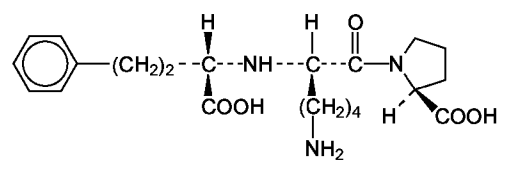
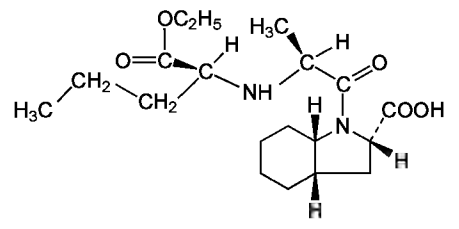
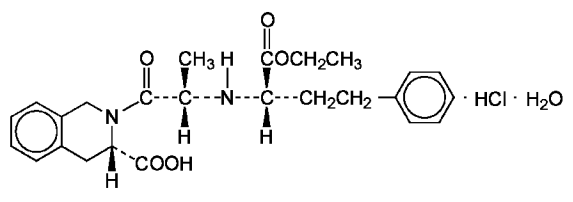
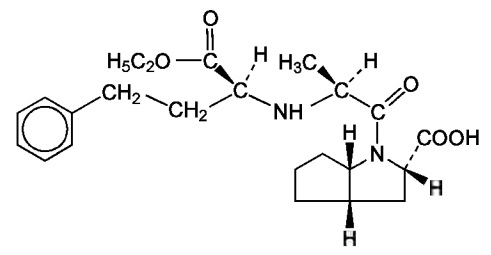
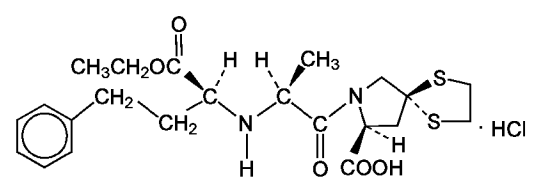
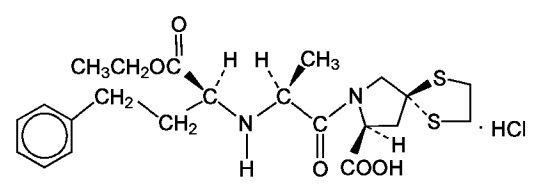
guanadrel, bretylium, debrisoquin, bethanidine

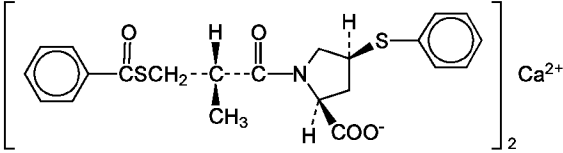
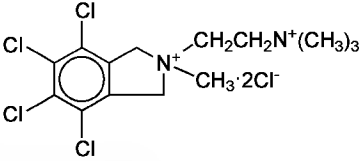
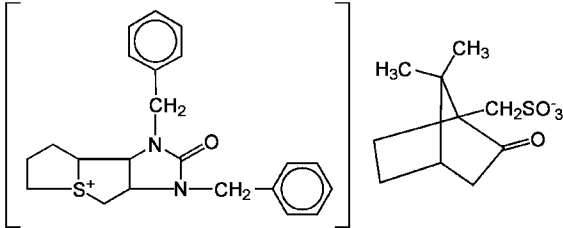
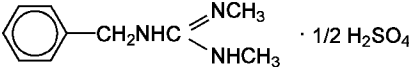
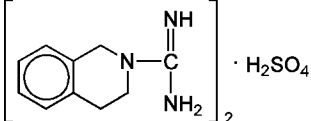
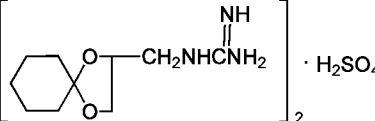
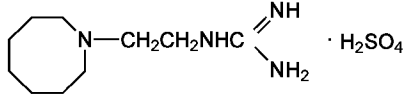
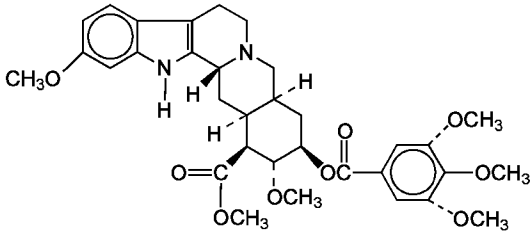
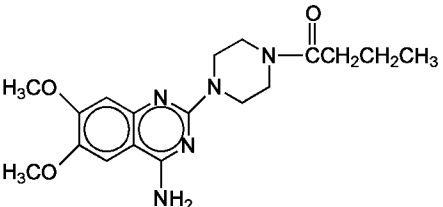
- Neuronal norepinephrine depleting agents
- reserpine
- α -Adrenoceptor blockers
- phentolamine
- prazosin
- terazosin
- doxazosin, bunazosin
- β -Adrenoceptor blockers
- propranolol
- metoprolol
- atenolol
- bisoprolol
- nadolol, acebutolol, pindolol, betaxolol, celiprolol, carvedilol, bucindolol, brefanolol
- α β -Adrenoceptor blockers
- labetalol
- Calcium Channel Blockers*
- verapamil
- diltiazem
- nifedipine
- nicardipine
- felodipine
- amlodipine
- nitrendipine
- isradipine
- lacidipine, benidipine
- Diuretics*
- Low ceiling diuretics
- hydrochlorothiazide, other thiazides
- chlorthalidone
- quinethazone
- metolazone
- High ceiling diuretics
- furosemide
- bumetanide
- ethacrynic acid
- Aldosterone antagonists
- spironolactone
- Potassium sparing diuretics
- triamterene
- amiloride
- Centrally Acting Agents*
- methyldopa
- clonidine
- guanabenz
- guanfacine
- rilmenidine
- Vasodilators*
- hydralazine
- minoxidil
- nitroprusside
- cadralazine
- Potassium Channel Openers*
- pinacidil
- cromakalim, lemakalim
- nicorandil
- diazoxide, minoxidil

Antihypertensive agents are shown in Table 6 (200–202).

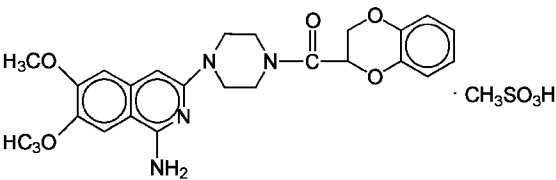
Table 6. Antihypertensive Agents

Generic name	CAS registry number	Molecular formula	Trade name	Structure
<i>Angiotensin converting enzyme inhibitors</i>				
alacepril	[74258-86-9]	C ₂₀ H ₂ N ₂ O ₅ S		
benazepril hydrochloride	[86541-74-4]	C ₂₄ H ₂₆ N ₂ O ₅ · HCl	Lotensin	

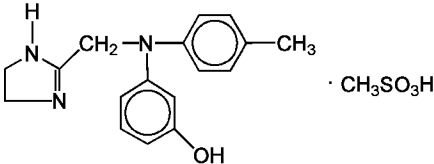
ceronapril	[111223-26-8]	C ₂₁ H ₃₃ N ₂ O P		
delapril hydrochloride	[83435-67-0]	C ₂ H ₃₃ ClN ₂ O ₅		
fosinopril sodium	[88889-14-9]	C ₃₀ H ₄₅ NNaO ₇ P	Monopril	
libenzapril	[109214-55-3]	C ₁₈ H ₂₅ N ₃ O ₅		
lisinopril (anhydrous)	[83915-83-7] [76547-98-3]	C ₂₁ H ₃₁ N ₃ O ₅ · 2H ₂ O	Prinivil, Zestril	
perindopril	[82834-16-0]	C ₁₉ H ₃₂ N ₂ O ₅		
quinapril hydrochloride monohydrate	[90243-99-5]	C ₂₅ H ₃₀ N ₂ O ₅ · HCl · H ₂ O		
ramipril	[87333-19-5]	C ₂₃ H ₃₂ N ₂ O ₅	Cardace	
spirapril hydrochloride	[94841-17-5]	C ₂₂ H ₃₀ N ₂ O ₅ S ₂ · HCl		
zofenopril calcium	[81938-43-4]	C ₂₂ H ₂₃ NO ₄ S ₂ · 1/2 Ca	Zoprace	

				
chlorisondamine chloride	[69-27-2]	C ₁₄ H ₂₀ Cl N ₂	<i>Ganglionic blockers</i> Ecolid	
hexamethonium bromide	[55-97-0]	C ₁₂ H ₃₀ Br ₂ N ₂	Bistrium	(CH ₃) ₃ N ⁺ (CH ₂) ₆ N ⁺ (CH ₃) ₃ •2Br
trimethaphan camsylate	[68-91-7]	C ₃₂ H ₄₀ N ₂ O ₅ S ₂	Arfonad	
bethanidine sulfate	[114-85-2]	C ₂₀ H ₃₂ N O ₄ S	<i>Neuronal blockers</i> Meobentine	
debrisoquin sulfate	[1131-64-2]	C ₂₀ H ₂₆ N O ₄ S	Declinax	
guanadrel sulfate	[40580-59-4]	C ₂₀ H ₄₀ N O ₈ S	Hylorel	
guanethidine monosulfate	[645-43-2]	C ₁₀ H ₂₄ N ₄ O ₄ S	Ismelin	
reserpine	[50-55-5]	C ₃₃ H ₄₀ N ₂ O ₉	<i>Neuronal norepinephrin depleting agents</i> Serpasil, Reserpoid	
bunazosin	[80755-51-7]	C ₁₉ H ₂₇ N ₅ O ₃	<i>α-Adrenoceptor blockers</i>	
doxazosin mesylate	[77883-43-3]	C ₂₄ H ₂₉ N ₅ O ₈ S		

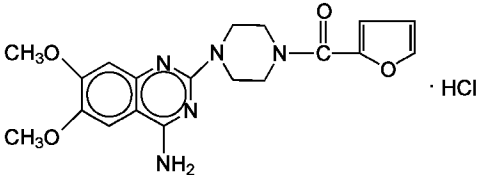
phentolamine mesylate [65-28-1] C₁₈H₂₃N₃O₄S Regitine



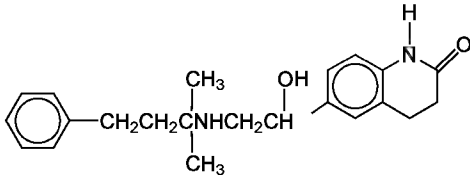
prazosin hydrochloride [19237-84-4] C₁₉H₂₂ClN₅O₄ Minipress



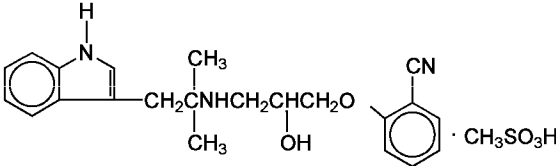
terazosin hydrochloride dihydrate [70024-40-7] C₁₉H₂₂ClN₅O₄ · 2H₂O Hytrin



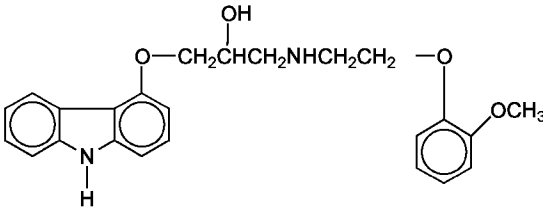
brefanolol [104051-20-9] C₂₂H₂₆N₂O₂ β -Adrenoceptor blockers



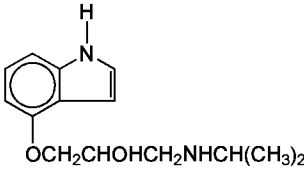
bucindolol hydrochloride [70369-47-0] C₂₂H₂₅N₃O₂ · HCl



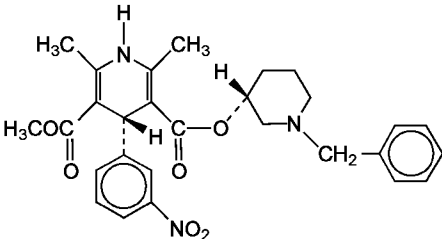
carvedilol [72956-09-3] C₂₄H₂₆N₂O₄



pindolol [13523-86-9] C₁₄H₂₀N₂O₂ Viskin



benidipine [105979-17-7] C₂₈H₃₁N₃O *Calcium channel blockers*



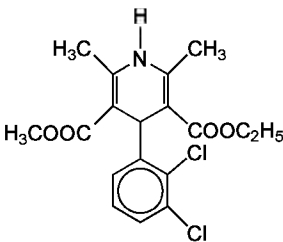
felodipine [72509-76-3] C₁₈H₁₉Cl₂NO₄

isradipine

[75695-93-1]

C₁₉H₂₁N₃O₅

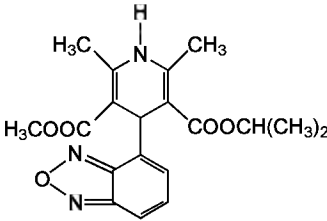
DynaCirc



lacidipine

[103890-78-4]

C₂₂H₃₃NO

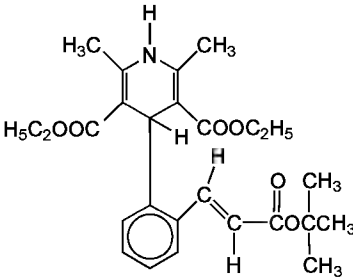


nitrendipine

[39562-70-4]

C₁₈H₂₀N₂O

Baypress

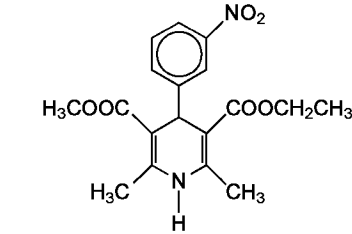


amiloride hydrochloride dihydrate

[17440-83-4]

C₁₈H₁₆Cl₂N₇O · 2H₂O

Diuretics
Midamor

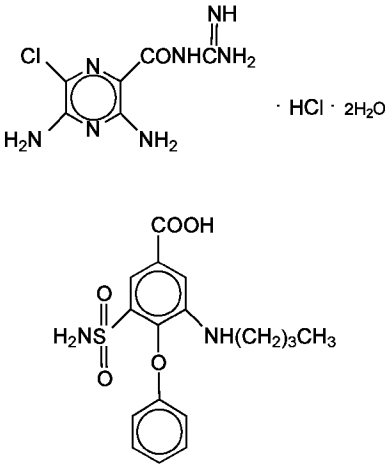


bumetanide

[28395-03-1]

C₁₇H₂₀N₂O₅S

Bumex

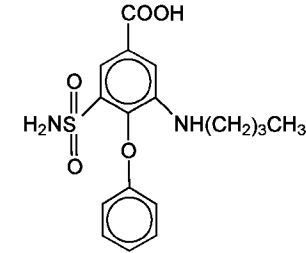


chlorthalidone

[77-36-1]

C₁₄H₁₁ClN₂O₄S

Hygroton

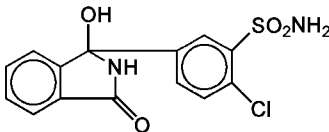


ethacrynic acid

[58-54-8]

C₁₃H₁₂Cl₂O₄

Edecrin

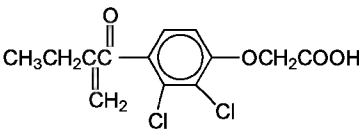


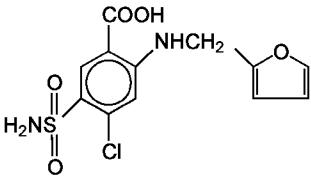
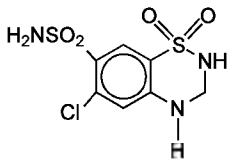
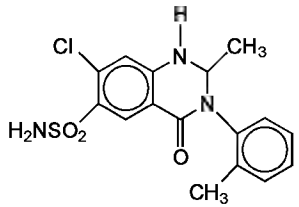
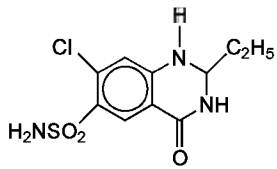
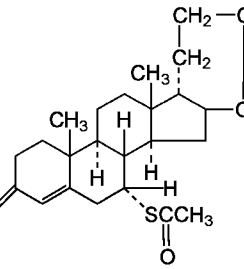
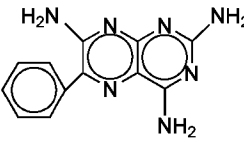
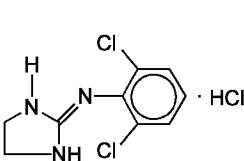
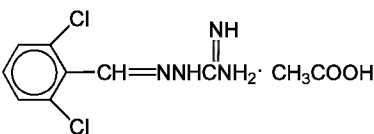
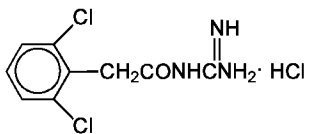
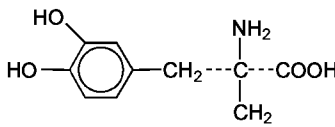
furosemide

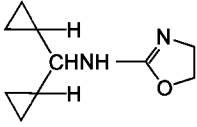
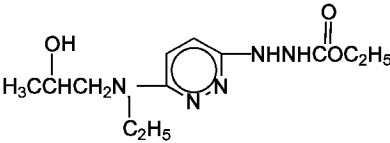
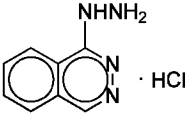
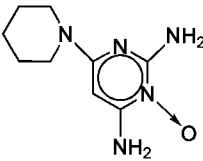
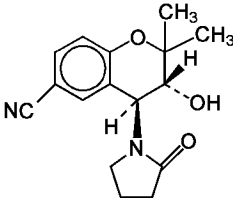
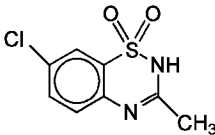
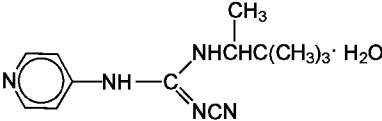
[54-31-9]

C₁₂H₁₁ClN₂O₅S

Lasix, Disal



				
hydrochlorothiazide	[58-93-5]	C ₇ H ₈ ClN ₃ O ₄ S ₂	Esidrix, HydroDiuril	
metolazone	[17560-51-9]	C ₁₁ H ₁₁ ClN ₃ O ₃ S	Zaroxolyn, Mykrox, Diulo	
quinethazone	[73-49-4]	C ₁₀ H ₁₂ ClN ₃ O ₃ S	Hydromox	
spironolactone	[52-01-7]	C ₂₄ H ₃₂ O ₄ S	Aldactone	
triamterene	[396-01-0]	C ₁₂ H ₁₁ N ₇	Dyrenium	
clonidine hydrochloride	[4205-91-8]	C ₉ H ₁₀ Cl ₃ N ₃	<i>Centrally acting antihypertensive agents</i> Catapres	
guanabenz acetate	[23256-50-0]	C ₁₀ H ₁₂ Cl ₂ N ₄ O ₂	Wytensin	
guanfacine hydrochloride	[29110-47-2]	C ₉ H ₁₀ Cl ₃ N ₃ O	Tenex	
methyl dopa	[555-30-6]	C ₁₀ H ₁₃ NO ₄	Aldomet	
rilmenidine	[54187-04-1]	C ₁₀ H ₁₁ N ₂ O		

				
cadralazine	[64241-34-5]	C ₁₂ H ₂₁ N ₅ O ₃	Vasodilators	
				
hydralazine hydrochloride	[304-20-1]	C ₈ H ₉ ClN ₄	Apresoline	
				
minoxidil	[38304-91-5]	C ₉ H ₁₅ N ₅ O	Loniten	
				
nitroprusside sodium dihydrate	[13755-38-9]	C ₅ FeN O ·2H ₂ O ·2Na	Nipride	Na ₂ [Fe(CN) ₅ NO]•2H ₂ o
cromakalim	[94470-67-4]		Potassium channel openers	
				
diazoxide	[364-98-7]	C ₈ H ₇ ClN ₂ O ₂ S	Hyperstat	
				
nicorandil	[65141-46-0]	C ₈ H ₉ N ₃ O ₄		
				
pinacidil	[85371-64-8]	C ₁₃ H ₁₉ N ₅ ·H ₂ O	Pindac	
				

Agents Affecting the Renin–Angiotensin System

The renin-angiotensin system (RAS) plays an important role in the regulation of arterial blood pressure in the body (203,204). The enzyme renin [9015-94-5], which is synthesized and released from the kidney, catalyzes the formation of angiotensin I [9041-90-1] a decapeptide, from the substrate angiotensinogen, an α₂-globulin, synthesized in the liver and released into the blood stream. ACE, a nonspecific carboxypeptidase, cleaves a dipeptide from the carboxyl terminal of angiotensin I to form angiotensin II [11128-99-7], an octapeptide. The blood vessels of the pulmonary circulation are the main site for this conversion. Angiotensin II is further cleaved to the heptapeptide, angiotensin III [12687-51-3] by the action of tissue aminopeptidase [9031-94-1]. Angiotensin II is the most potent product of this cascade. Angiotensin I is relatively inactive, whereas angiotensin III is less potent than angiotensin II as a vasoconstrictor but is as active as angiotensin II in stimulating the release of aldosterone [52-39-1], C₂₁H₂₈O₅.

The primary effects of angiotensin II are (1) producing vasoconstriction directly or indirectly through activation of the adrenergic nervous system; (2) eliciting cardiac stimulation; (3) stimulating aldosterone and vasopressin secretion; and (4) evoking dipsogenesis. All these actions, directly or indirectly, produce elevation of blood pressure (203). Theoretically, renin inhibitors, ACE inhibitors, and angiotensin II receptor antagonists can be potent antihypertensive agents.

Angiotensin Converting Enzyme (ACE) Inhibitors. ACE inhibitors are very efficacious in reducing high blood pressure. The antihypertensive activity is better correlated with the vascular tissue ACE inhibition than plasma ACE inhibition. Plasma ACE activity returns to predrug level while significant lowering of the blood pressure is still being observed. Teprotide [35115-60-7], a nonapeptide ACE inhibitor, was demonstrated to have potent antihypertensive effects after iv administration. The drawback of teprotide is lack of oral activity. Captopril (Table 4), a sulfhydryl containing small molecule, was the first practical nonpeptide ACE inhibitor in humans (205). Then came enalapril (Table 4) and lisinopril (206), the nonsulfhydryl

containing ACE inhibitors (202).

ACE inhibitors are used in the first-line therapy of hypertension (207–213). Initially it was thought that ACE inhibitors were efficacious only in patients having high plasma renin activity (PRA) such as in renal or malignant hypertension. Captopril, however, was found to be efficacious in patients having essential hypertension, particularly those with high or moderately high PRA. Only about 20% of patients having essential hypertension have high to moderately high PRA, but ACE inhibitor used as monotherapy is effective in 50–60% of all patients. The reason may be that many other antihypertensive drugs (such as diuretics), calcium channel blockers, and a low salt diet activate the RAS and patients become renin dependent and are responsive to drugs affecting the RAS (214), such as ACE inhibitors, renin inhibitors, and angiotensin II receptor antagonists.

ACE inhibitors lower the elevated blood pressure in humans with a concomitant decrease in total peripheral resistance. Cardiac output is increased or unchanged; heart rate is unchanged; urinary sodium excretion is unchanged; and potassium excretion is decreased. ACE inhibitors promote reduction of left ventricular hypertrophy.

Other mechanisms of action, such as potentiation of the bradykinin [58-82-2], $C_{50}H_{73}N_{15}O_{11}$, effect, and increased production of prostaglandins have been reported to explain, in part, the antihypertensive effects of ACE inhibitors during chronic therapy (215,216). The inhibition of angiotensin II production is considered the primary, if not the only, mechanism of action of ACE inhibitors, even though the circulating angiotensin II levels may not accurately reflect the situation. Headache, dizziness, fatigue, skin rash, and cough are the most common side effects of ACE inhibitors. Cough in patients treated with an ACE inhibitor is considered to be caused by the build-up of bradykinin and prostaglandins. ACE is thought to be the same enzyme that catabolizes bradykinin.

Angiotensin II Receptor Antagonists. Many potent peptide angiotensin II receptor antagonists were known before the advent of the ACE inhibitors, but none were active after oral administration. One such peptide, saralasin [34273-10-4], $C_{42}H_{55}N_{13}O_{10}$, was approved for use in humans as a diagnostic tool. In addition to antagonistic effects, saralasin produces an initial agonist (hypertensive) action, even though it is much weaker than angiotensin II. The lack of oral efficacy and its intrinsic agonistic effects make saralasin an impractical drug.

The patent literature contains a series of nonpeptide imidazole derivatives that had angiotensin II receptor antagonistic effects (217). These compounds were found to be weak angiotensin II receptor antagonists (218,219), yet they were competitive antagonists, suggesting that a small nonpeptide molecule could compete with the octapeptide, angiotensin II, for the active site of the receptor. Several nonpeptide angiotensin II receptor antagonists have been synthesized, some of which are shown in Figure 3. DuP 753 is a potent orally active drug in clinical trials (220,221); L-158,809 has been reported to be 100–180 times more potent than DuP 753 as an angiotensin II receptor antagonist (222). The spectrum of antihypertensive activity should be similar to that of the ACE inhibitors, but with different side effects because the angiotensin II receptor antagonists do not potentiate the action of bradykinin.

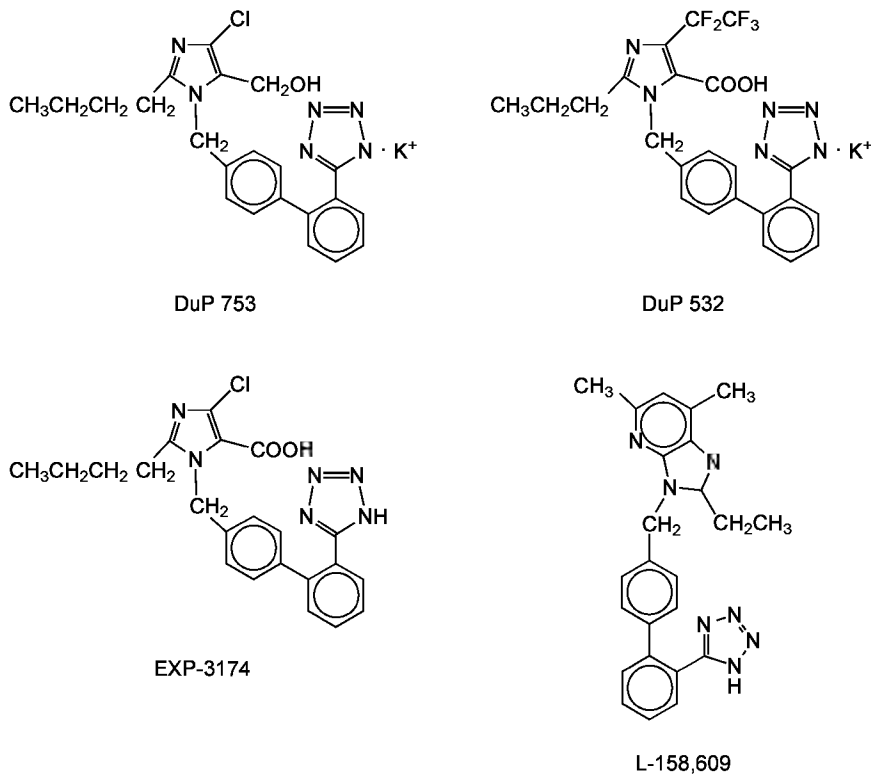


Fig. 3. The Angiotensin II receptor antagonists.

Renin Inhibitors. Renin catalyzes the first and rate limiting step of the RAS and is very specific for the conversion of angiotensinogen to angiotensin I. Although renin inhibitors have been large molecules, particularly renin antibodies, and not orally active (203,223), several dipeptide and dipeptide transition-state compounds have been reported to inhibit renin activity and lower blood pressure in humans following iv administration. However, there is no indication that any of these compounds are orally active at reasonably low doses (202,203,224–226). The transition-state inhibitors are stable structures resembling the transition state of the enzyme reaction and are bound more tightly to renin than renin is to the substrate.

In animal models, renin inhibitors after iv administration have been shown to be equally efficacious as compared to ACE inhibitors in lowering blood pressure, and to have similar effects on the cardiovascular and renal parameters. Some of the renin inhibitors tested are enalkiren (A-64662), CGP 38 560A, CP 71362, KRI-1230, U-71039, ES6864, and PD-134672. The structures of enalkiren and the formula for PD-134672 are shown in Figure 4.

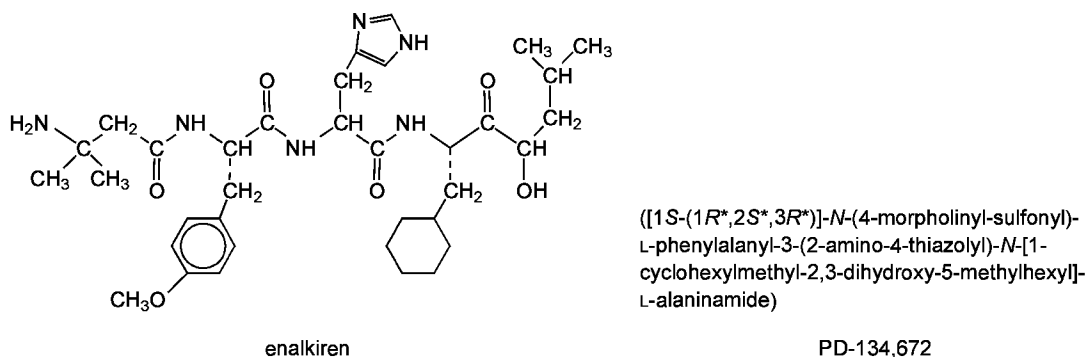


Fig. 4. Renin inhibitors.

Agents Affecting the Adrenergic Nervous System

Historically, the vasopressor systems, particularly the adrenergic nervous system, drew the most attention in hypertension research and many drugs affecting this system have been introduced. An agent achieves antagonism of this system either by decreasing the number of nerve impulses traveling down the nerves, by blocking ganglia, by blocking the release of the adrenergic neurotransmitter, norepinephrine, by depleting the norepinephrine stores in the neurons, or by blocking the adrenoceptors in the blood vessels. Vascular tone is maintained mainly by the adrenergic nervous system, and decreasing the tone by any of these mechanisms causes a lowering of blood pressure.

Ganglionic Blockers. Ganglionic blocking agents (see Table 6), such as hexamethonium, trimethaphan, and chlorisondamine, block the autonomic ganglia and thus decrease sympathetic outflow. Tolerance develops quickly to these agents. Because of such disturbing side effects as severe orthostatic hypotension, sexual dysfunction, dry mouth, and urinary retention, these drugs have become obsolete.

Adrenergic Neuronal Blockers. The adrenergic neuronal blocking agents, guanethidine, bretylium, debrisoquin, and guanadrel (Table 6), produce hypotension by blocking the release of norepinephrine from the nerve terminals of adrenergic neurons. These drugs are taken up by the neurons and decrease sympathetic tone, heart rate, cardiac output, and total peripheral resistance. Some deplete norepinephrine stores and thus produce an initial sympathomimetic response increasing these various responses. Orthostatic hypotension, severe sexual dysfunction and impairment, fluid retention, and diarrhea are the primary side effects of this class of agents which is obsolete and used only when no other agents work.

Neuronal Norepinephrine Depleting Agents. Reserpine (Table 6) is the most active alkaloid derived from *Rauwolfia serpentina*. The principal antihypertensive mechanism of action primarily results from depletion of norepinephrine from peripheral sympathetic nerves and the brain adrenergic neurons. The result is a drastic decrease in the amount of norepinephrine released from these neurons, leading to decrease in vascular tone and lowering of blood pressure. Reserpine also depletes other transmitters including epinephrine, serotonin [50-67-9], C₁₀H₁₂N₂O, and dopamine [51-61-6], C₈H₁₁NO₂ (see NEUROREGULATORS). Reserpine is efficacious in all forms of hypertension, particularly with the concomitant use of a thiazide diuretic. The most serious side effect is mental depression. Other side effects include nasal congestion, sedation, drowsiness, lethargy, decreased libido, impotence, and nightmares.

α-Adrenoceptor Blockers. Nonselective α-adrenoceptor blockers (Table 6), such as phentolamine, which block both α₁- and α₂-adrenoceptors, produce vasodilation by antagonizing the effects of endogenous norepinephrine. They also produce severe tachycardia and have been replaced by selective α₁-adrenoceptor blockers, such as prazosin, terazosin, and doxazosin, which do not usually cause severe tachycardia.

Prazosin, a selective α₁-adrenoceptor antagonist, exerts its antihypertensive effect by blocking the vasoconstrictor action of adrenergic neurotransmitter, norepinephrine, at α₁-adrenoceptors in the vasculature (200,227,228). Prazosin lowers blood pressure without producing a marked reflex tachycardia. It causes arteriolar and venular vasodilation, but a significant side effect is fluid retention. Prazosin increases HDL cholesterol, decreases LDL cholesterol, and does not cause glucose intolerance.

Doxazosin, a prazosin derivative, is a highly selective α₁-adrenoceptor blocker (229,230). It has no significant antagonistic effects on presynaptic or postsynaptic α₂-adrenoceptors. Blocking activation of α₁-adrenoceptors prevents the breakdown of phosphatidylinositol and the resulting vasoconstriction. Lowering of blood pressure by doxazosin is not accompanied by an increase in heart rate or cardiac output. Its duration of action is as long as 24 h. Doxazosin in chronic hypertension treatment reduces total cholesterol, LDL cholesterol, and triglyceride levels, and increases HDL cholesterol.

Terazosin is selective α₁-adrenoceptor blocker having hypotensive efficacy equal to that of prazosin. Terazosin has a longer duration of action and better gastrointestinal absorption profile than prazosin.

β-Adrenoceptor Blockers. There is no satisfactory mechanism to explain the antihypertensive activity of β-adrenoceptor blockers (see Table 1) in humans particularly after chronic treatment (228,231–233). Reductions in heart rate correlate well with decreases in blood pressure and this may be an important mechanism. Other proposed mechanisms include reduction in PRA, reduction in cardiac output, and a central action. However, pindolol produces an antihypertensive effect without lowering PRA. In long-term treatment, the cardiac output is restored despite the decrease in arterial blood pressure and total peripheral resistance. Atenolol (Table 1), which does not penetrate into the brain is an efficacious antihypertensive agent. In short-term treatment, the blood flow to most organs (except the brain) is reduced and the total peripheral resistance may increase.

Better antihypertensive effect of β-adrenoceptor blockers is found in patients having high PRA and most are not efficacious in patients having low PRA or in elderly patients. β-Adrenoceptor blockers usually lower arterial blood pressure about 10 mm Hg (1.3 kPa). Side effects include lethargy, dyspnea, nausea, dizziness, headache, impotency, cold hands and feet, vivid dreams and nightmares, bronchospasm, bradycardia, and sleep disturbances.

β-Adrenoceptor blockers for the treatment of hypertension include: (1) the cardioselective β₁-adrenoceptor blockers without intrinsic sympathomimetic activity (ISA), ie, atenolol (Table 3), bisoprolol (Table 3), and metoprolol (Table 1); (2) the cardioselective with ISA, ie, acebutolol (Table 1); (3) the noncardioselective without ISA, ie, propranolol (Table 1) and timolol [26839-75-8], C₁₃H₂₄N₄O₃S; and (4) the noncardioselective with ISA, ie, oxprenolol [6452-71-7], C₁₅H₂₃NO₃, and pindolol.

α- and β-Adrenoceptor Blocking Agents. Labetalol possesses both α- and β-adrenoceptor blocking effects, blocking both β₁- and β₂-adrenoceptors, but only α₁-adrenoceptors (234,235). It also possesses β₂-adrenoceptor agonistic (vasodilatory) effects, and produces significant reduction in blood pressure and a slight decrease in heart rate. It is efficacious in mild, moderate, and severe hypertension. The cardiac output is maintained because of an increase in stroke volume. Exercise-induced blood pressure increases are blunted and the heart rate is reduced. In chronic treatment, PRA is reduced. Labetalol does not influence the blood cholesterol, triglyceride, or lipoproteins. The side effects are gastrointestinal discomfort and dizziness.

Calcium Channel Blockers

The extracellular concentration of calcium is approximately 2,500 to 25,000 times higher than that of intracellular calcium, 2.5 mM vs 0.1 to 1.0 μM. This gradient is maintained by regulating the calcium influx through receptor as well as voltage operated channels. Voltage operated channels are divided into three subtypes: L, N, and T. Calcium channel blockers, such as verapamil (Table 1), diltiazem (Table 3), or nifedipine (Table 3) only block the L-type channels. Contraction of vascular smooth muscle is governed by the intracellular free calcium, regulated by the voltage operated calcium channels. When the channels are open, the extracellular calcium moves in the cell across the membrane through a great electrochemical gradient. The process initiates the contraction.

Another mechanism in initiating the contraction is agonist-induced contraction. It results from the hydrolysis of membrane phosphatidylinositol and the formation of inositol triphosphate (IP₃). IP₃ in turn triggers the release of intracellular calcium from the sarcoplasmic reticulum and the influx of more extracellular calcium. The third mechanism in triggering the smooth muscle contraction is the increase of calcium influx through the receptor-operated channels. The increased cytosolic calcium enhances the binding to the protein, calmodulin [73298-54-1].

Calcium channel blockers reduce arterial blood pressure by decreasing calcium influx, resulting in a decrease in intracellular calcium (236,237). The arterial smooth muscle tone decreases, thereby decreasing total peripheral resistance. The increase in vascular resistance in hypertension is found to depend much on calcium influx. Calcium channel blockers reduce blood pressure at rest and during exercise. They decrease the transmembranous calcium influx or entry that lead to a net decrease of intracellular calcium and therefore the vascular tone falls, as does blood pressure.

In addition to the vascular effects, calcium channel blockers (Table 6) such as isradipine, nifedipine (Table 3), and nitrendipine, produce natriuretic

effects by increasing fractional sodium excretion and free water clearance. They also reduce distal tubular sodium reabsorption.

Calcium channel blockers normalize the blood pressure in about 80% of hypertensive patients older than 60 years of age, 50% of those between 40 and 60 years of age, and only 20% of patients under 40 years of age. Thus calcium channel blockers are best for patients who are elderly and have low PRA and mostly ineffective in patients who have high PRA. This responsiveness profile is very similar to that of the diuretics.

Nifedipine, verapamil, and diltiazem are all efficacious in the treatment of mild and moderate hypertension, but nifedipine is more efficacious than diltiazem and verapamil in the control of severe hypertension. Nifedipine does not cause significant reflex tachycardia or orthostatic hypotension. Nifedipine benefits the older and black patients and patients with low PRA.

Calcium channel blockers cause more pronounced lowering of blood pressure in hypertensive patients than in normotensive individuals. Generally, all calcium channel blockers cause an immediate increase in PRA during acute treatment in patients having hypertension but PRA is normalized during chronic treatment despite the sustained decrease in blood pressure. These agents also do not generally produce sodium and water retention, unlike the conventional vasodilators. This is because they produce diuretic effects by direct actions on the kidney.

It has been suggested that in a large subset of hypertensive patients there is a slight but constant increase of traffic of free calcium influx and as a result there is an increase of intracellular free calcium leading to additional release of calcium from intracellular storage sites. The end result is a slight but chronic increase in vascular tone and peripheral resistance. Over time, constant adaptation of this slight increase of vascular tone inches the arterial blood pressure up to the hypertensive level. Calcium channel blockers block the inward movement of calcium into the cells of vascular smooth muscles, and are thus considered to be the drugs that correct the fundamental abnormalities of hypertension. Calcium channel blockers have been shown in animal experiments to prevent and cause regression of atherosclerosis (238,239).

Verapamil (Table 1), the first slow channel calcium blocker synthesized to selectively inhibit the transmembrane influx of calcium ions into cells, lowers blood pressure in hypertensive patients having good organ perfusion particularly with increased renal blood flow. Sustained-release verapamil for once a day dosing is available for the treatment of hypertension. Constipation is a prominent side effect. Headache, dizziness, and edema are frequent and verapamil can sometimes cause AV conduction disturbances and AV block. Verapamil should not be used in combination with β -adrenoceptor blockers because of the synergistic negative effects on heart rate and contractile force.

Nifedipine (Table 3) is a potent vasodilator that selectively dilates resistance vessels and has fewer effects on venous vessels. It does not cause reflex tachycardia during chronic therapy. Nifedipine is one of the first-line choices for black or elderly patients and patients having concomitant angina pectoris, diabetes, or peripheral vascular diseases. Nifedipine, sublingually, is also suitable for the treatment of hypertensive emergencies. Nifedipine does not impair sexual function or worsen blood lipid profile. The side effects are flushing, headache, and dizziness.

Diltiazem inhibits calcium influx via voltage-operated channels and therefore decreases intracellular calcium ion. This decreases smooth muscle tone. Diltiazem dilates both large and small arteries and also inhibits α -adrenoceptor activated calcium influx. It differs from verapamil and nifedipine by its use dependence. In order for the blockade to occur, the channels must be in the activated state. Diltiazem has no significant affinity for calmodulin. The side effects are headache, edema, and dizziness.

Diuretics

The principal mechanism of the hypotensive effect of diuretics (qv) is salt and fluid depletion, leading to reduction in blood volume (200,240). Acute effects lead to a decrease in cardiac output and an increase in total peripheral resistance. However, during chronic administration, cardiac output and blood volume return toward normal and total peripheral resistance decreases to below pretreatment values. As a result, the blood pressure falls. The usual reduction in blood volume is about 5%. A certain degree of sustained blood volume contraction has to occur before the blood pressure decreases. The usual decrease in blood pressure achieved using a diuretic is about 20–10 mm Hg (2.7–1.3 kPa) (systolic–diastolic pressures).

Intake of a large amount of sodium chloride negates the antihypertensive effects of diuretics. Other mechanisms, such as direct vasodilating action, decreased responsiveness to vasopressor agents, stimulation of prostacyclin [35121-78-9], C₂₀H₃₂O₅, production, and reduction in the intracellular calcium concentration, etc, only play a minor role in the overall antihypertensive effects of diuretics.

Diuretics, such as those of the thiazide type, have been the cornerstone of first-line antihypertensive treatments for decades. However, popularity and use have eroded as a result of increases in sudden death in patients on diuretic therapy, and unfavorable effects on blood lipids profile, ie, increasing cholesterol and triglyceride. These effects have been implicated as possible causes for the lack of decrease in the mortality rate resulting from acute MI in patients treated with a diuretic (187,240,241). However, diuretics do protect against stroke and CHF.

Diuretics are needed to return to normal the expanded extracellular volume that other antihypertensive agents produce, such as fluid retention and blood volume expansion, via compensatory mechanisms of the body. The loss of efficacy of antihypertensive agents can be restored if a diuretic is used concomitantly. In the treatment of hypertension, high ceiling or loop diuretics, such as furosemide, ethacrynic acid, and bumetanide, are no more efficacious than the thiazide-type of diuretics. In fact, these agents cause more side effects, such as dehydration, metabolic alkalosis, etc, and therefore, should not be used except in situations where rapid elimination of fluid volume is clearly indicated.

Diuretics can cause hypokalemia, hyperglycemia, and hyperuricemia. After long-term treatment they may increase serum triglyceride and cholesterol (242).

Aldosterone Antagonists. Spironolactone is a competitive antagonist of aldosterone and is effective in lowering the the hypertension not only of patients having primary aldosteronism, but also of many patients having essential hypertension whose aldosterone levels are not elevated. It is particularly efficacious in patients having low PRA. The mechanism of action is by antagonizing the sodium-retaining and potassium-wasting effects of aldosterone at the Na⁺–K⁺ exchange sites of the renal distal tubule. Spironolactone prevents or reverses hypokalemia in patients treated with the low and high ceiling diuretics.

Gynecomastia may be associated with the use of spironolactone and is reversible upon withdrawal of the drug.

Potassium Sparing Diuretics. Triamterene and amiloride, potassium sparing diuretics, by themselves produce only slight antihypertensive effects. The main use is to prevent or to treat the hypokalemia induced by thiazide-type and high ceiling loop diuretics, such as furosemide and bumetanide.

Centrally Acting Agents

Clonidine, methyl dopa (α -methyl dopa), guanabenz, and guanfacine lower arterial blood pressure by activating the α_2 -adrenoceptors in the pontomedullary region of the brain (200). The central hypotensive activity is blocked by α -adrenoceptor blockers, such as phentolamine [50-60-2], C₁₇H₁₉H₅O, and yohimbine [146-48-5], C₂₁H₂ N₂O₃. Side effects include drowsiness, sedation (except rilmenidine [S3341]), dry mouth, sexual dysfunction, and depression. Tricyclic antidepressants, such as imipramine [50-49-7], C₁₉H₂₄N₂, and desipramine [50-47-5], C₁₈H₂₂N₂, are known to counteract the central antihypertensive effects of clonidine (see PSYCHOPHARMACOLOGICAL AGENTS).

Methyl dopa. Methyl dopa reduces arterial blood pressure by decreasing adrenergic outflow and decreasing total peripheral resistance and heart rate having no change in cardiac output. Blood flow to the kidneys is not changed and that to the heart is increased. It causes regression of myocardial hypertrophy.

Methyl dopa, through its metabolite, α -methylnorepinephrine formed in the brain, acts on the postsynaptic α_2 -adrenoceptor in the central nervous system. It reduces the adrenergic outflow to the cardiovascular system, thereby decreasing arterial blood pressure. If the conversion of methyl dopa to α -methylnorepinephrine in the brain is prevented by a dopamine β -hydroxylase inhibitor capable of penetrating into the brain, it loses its antihypertensive effects.

Methyl dopa is effective in mild, moderate, and severe hypertension but a thiazide-type diuretic is needed to overcome the fluid retaining side effect. Methyl dopa has been shown to prevent and induce regression of ventricular hypertrophy in hypertensive patients. The principal side effects are sedation, drowsiness, nasal congestion, fluid retention, and in rare occasions, hemolytic anemia.

Clonidine. Clonidine decreases blood pressure, heart rate, cardiac output, stroke volume, and total peripheral resistance. It activates central α_2 -adrenoceptors in the brainstem vasomotor center and produces a prolonged hypotensive response. Clonidine, most efficaciously used concomitantly with a diuretic in long-term treatment, decreases renin and aldosterone secretion.

When clonidine is withdrawn abruptly, patients may experience a rebound hypertensive phenomenon, wherein blood pressure rises rapidly to a level higher than the predrug level. These patients may experience symptoms of headache, tachycardia, agitation, and nervousness. If rebound hypertension occurs, resumption of clonidine therapy or administration of phentolamine reduces the blood pressure. For clonidine withdrawal, the dose should be reduced gradually over a two-week period. The principal side effects are sedation, dry mouth, drowsiness, dizziness, and fatigue.

Guanabenz. Guanabenz has been shown to be efficacious in mild and moderate hypertension. Sympathetic tone is decreased with a resultant decrease in total peripheral resistance. In hypertensive patients, guanabenz tends to decrease heart rate and very seldom causes severe fluid retention. It does not suppress PRA but it has a cholesterol and triglyceride lowering effect in chronic therapy. Guanabenz does not cause glucose intolerance, so it is suitable to be used in diabetic patients. The principal side effects are sedation, dry mouth (1 in 4 patients), asthenia, and dizziness. Rebound hypertensive syndrome also occurs in patients experiencing abrupt discontinuation of guanabenz.

Guanfacine. Guanfacine, used in patients having mild to moderate hypertension, can lower blood pressure 50–25 mm Hg (systolic–diastolic) in hypertensive patients. Side effects such as sedation, dry mouth, and asthenia are less as compared to those of guanabenz and clonidine. Guanfacine reduces blood cholesterol and triglyceride and does not cause glucose intolerance.

Rilmenidine. Rilmenidine is a central α_2 -adrenoceptor agonist and has been shown to be a potent centrally acting antihypertensive agent without the prominent side effect of sedation.

Vasodilators

Vasodilators dilate or relax the smooth muscles of the vasculatures directly or indirectly by releasing endogenous vasodepressors or antagonizing the endogenous vasopressors or vasopressor systems (200,243,244). Vasodilators may interfere with the entry, intracellular release, and utilization of calcium, the activation of the protein kinase C system, cGMP formation, and EDRF turnover.

Hydralazine. Hydralazine causes vasodilation in all primary vascular beds and has more pronounced effects on capacitance than on resistance blood vessels. Despite the hypotension it produces, hydralazine increases renal blood flow and cardiac output. PRA increases with its use. Tachycardia, headache, dizziness, and water and sodium retention are principal side effects of hydralazine therapy.

Diazoxide. Diazoxide, chemically related to the thiazide diuretics, is a vasodilator having no diuretic effects. In fact, diazoxide causes marked salt and water retention. It has been suggested that diazoxide has potassium channel opener effects. Because of rapid protein binding, diazoxide has to be given by rapid intravenous injection. Its use is limited to the treatment of hypertensive emergencies or crises. Diazoxide causes marked tachycardia, increases PRA, and causes hyperglycemia.

Minoxidil. Minoxidil is one of the most potent vasodilators available for the treatment of hypertension. Minoxidil is a potassium channel opener acting directly on the smooth muscle of the arterioles to decrease peripheral resistance and blood pressure. In long-term treatment, minoxidil causes severe fluid retention, tachycardia, and hair growth (hirsutism). It stimulates the adrenergic nervous system and the renin-angiotensin system. Because of side effects, minoxidil is reserved for use in hypertensive patients having renal failure or in patients having hypertension that is refractory to other antihypertensive drugs.

Nitroprusside. Nitroprusside is a potent, fast-acting vasodilator that has to be administered intravenously by infusion. It relaxes arterial and venous vascular smooth muscle. Its use is mainly in hypertensive crises. Its effects terminate as soon as infusion of the drug is stopped.

Potassium Channel Openers

The resting membrane potential of most excitable cells is around –60 to –80 mV. This gradient is maintained by the activity of various ion channels. When the potassium channels of the cell open, potassium efflux occurs and hyperpolarization results. This decreases calcium channel openings, which in turn prevents the influx of calcium into the cell leading to a decrease in intracellular calcium in the smooth muscles of the vasculature. The vascular smooth muscles then relax and the systemic blood pressure falls.

Vasodilators having potassium channel opener activity relax smooth muscle in low (5–20 mM) K⁺ concentration but not in high (>80 mM) K⁺ solution, and glibenclamide [10238-21-8] should be able to reverse the induced relaxation (242,245–249). They also increase potassium efflux.

There are at least 13 primary types of K⁺ channels known. In addition, within each type there are several subtypes. The best known chemical classes of potassium channel openers are nicorandil, pinacidil, and cromakalim. They are all potent smooth muscle relaxants. Pharmacologically, they behave as classical vasodilators, lowering blood pressure and causing tachycardia and fluid retention.

Nicorandil. Nicorandil is a potassium channel opener that can lower blood pressure 21, 20, and 29 mm Hg after single oral doses of 10, 20, and 30 mg, respectively (250). There are no significant changes in heart rate. Headache is the primary side effect. Nicorandil has potent coronary vasodilator effects. It causes sustained vasodilation of arteriolar resistance and venous capacitance blood vessels, thus reducing cardiac preload and afterload.

Pinacidil. Pinacidil is a potent vasodilator, acting through potassium channel opening effects (242,251–253). Its antihypertensive effect is greater than that of hydralazine and prazosin in chronic treatment. Its fast onset of action also makes it suitable for use in hypertensive crisis.

Pinacidil has a short half-life and most human studies were carried out in slow-release formulations. The reduction in blood pressure produced by pinacidil is accompanied by tachycardia and fluid retention. Plasma catecholamines and renin activity are increased. Other side effects are headache, dizziness, and asthenia.

Cromakalim. Cromakalim has a long half-life (254). Cromakalim at an oral dose of 1.5 mg in humans significantly lowers blood pressure 19–12 mm Hg (systolic–diastolic pressure). It increases renal blood flow, PRA, and heart rate. Cromakalim has bronchodilating activity that is beneficial for hypertensive asthmatic patients. Because of some undesirable effects seen in cardiac papillary muscles of animals on long-term treatment, future clinical trials are to be carried out using the active enantiomer, lemakalim (BRL 38227).

THROMBOLYTIC AGENTS

It has been well documented that the primary cause of acute myocardial infarction (AMI) is coronary arterial thrombosis (255). Thrombosis formation occurs at sites of ulcerated or fissured atheromatous plaques in the coronary circulation (256,257). Reperfusion of the coronaries to the ischemic infarcted area within 6 h after the onset of AMI can salvage the myocardium and limit infarct size (258–260). Furthermore, the better the preservation of the ventricular function, the better the survival rate. Progressive irreversible myocardiac damage occurs 30 min after ischemia starts. Therefore, the faster the coronary arterial thrombus is lyzed, the less irreversible damage done on the myocardium. It is imperative that once an AMI is diagnosed, iv thrombolytic agent should be administered as quickly as possible.

The success of thrombus lysis depends mainly on how large the thrombus is and whether any blood flow still remains. The outcome is better the larger the surface of the entire thrombus exposed to the thrombolytic agent. As the clot ages, the polymerization of fibrin cross-linking and other blood materials increases and it becomes more resistant to lysis. Therefore, the earlier the thrombolysis therapy starts, the higher the frequency of clot dissolution. Thrombolytic agents available are listed in Table 7 (261–276).

Table 7. Thrombolytic Agents

Generic name	CAS Registry Number	Trade name
tissue plasminogen activator (alteplase t-PA)	[105857-23-6]	Activase
streptokinase	[9002-01-1]	Streptase,

urokinase	[9039-53-6]	Kabikinase Abbokinase, Breokinase, Win-kinase
anisoylated plasminogen-streptokinase activator (APSAC, anistreplase)	[81669-57-0]	Eminase
prourokinase (scu-PA)	[82657-92-9]	Sandolase

Streptokinase, prourokinase, and APSAC are indirect plasminogen activators, whereas t-PA and urokinase are direct plasminogen activators. All these activators convert the formation of the active proteolytic enzyme plasmin [9001-90-5] from the proenzyme, plasminogen [9001-91-6] by cleaving the Arg₅-Val₁ bond. After iv administration, all five thrombolytic agents achieve approximately the same incidence of reperfusion rate (60–70%) if used optimally. t-PA and prourokinase require simultaneous heparin [9005-49-6] administration when used; the other thrombolytics do not. Reocclusion rate is higher with t-PA if heparin use is not maximized. The half-life is short (5–8 min) using t-PA and prourokinase, medium (16–23 min) using urokinase and streptokinase, and long (105 min) using APSAC. When used at efficacious doses, each has similar degrees of bleeding complications. The least expensive thrombolytic agent is streptokinase, which is about one-tenth of the others. No single agent is superior when all factors are taken into consideration. Whereas t-PA is clot selective, it has a very short half-life and simultaneous use of heparin is required. Bleeding is therefore as much of a problem with t-PA as the less clot selective agent, such as streptokinase. Streptokinase causes severe systemic fibrinogen degradation leading to extensive hypofibrinogenemia. Under this condition, reocclusion is less and the dissolution of the thrombus is more complete. This may explain why streptokinase has been shown, in most studies, to be as efficacious as t-PA. The most recent comparison study reporting the equal efficacy of t-PA, APSAC, and streptokinase tends to confirm this point. Most large trials show these agents reduce patient mortality from 16 to 30%.

The dosage of each thrombolytic agent should be high enough to produce a lysis state long enough for complete clot dissolution to occur. Aspirin, a platelet aggregation inhibitor, has been demonstrated to decrease mortality of AMI by itself and to further decrease that of the thrombolytic agents if used concomitantly (277–279). The use of combinations of aspirin, heparin, vasodilator, and the thrombolytic agent decreases the incidence of rethrombosis.

Tissue-Type Plasminogen Activator (t-PA). t-PA is a physiologic activator of plasminogen in the body. It is a protein containing 527 amino acids having mol wt ~64,000, and is mainly produced in the endothelial cells lining blood vessels. It is also made in the liver, spleen, lungs, muscle, and other tissues. The commercial preparation derives from biotechnological cloning and production techniques, ie, it is recombinant t-PA (see GENETIC ENGINEERING; PROTEIN ENGINEERING). t-PA can occur in either a one- or two-chain form. Both forms are active but the two-chain form is longer acting (261,264,266,280–283).

t-PA has a much higher affinity for fibrin and fibrin-bound plasminogen as compared to the circulating plasminogen. For this reason, under normal conditions generalized (systemic) fibrinogenolysis in the circulation is thought not to occur. However, in the treatment of AMI, the large amount of t-PA used and infused for a prolonged period causes generalized fibrinogenolysis because of the activation of circulating plasminogen. In the treatment of AMI, a bolus intravenous injection of 10 mg is followed by an iv infusion of 50 mg/h for one hour and 20 mg/h for two hours. The half-life of t-PA in the circulation is about 4–5 min. It is cleared by the liver. The activation of plasminogen by t-PA is accelerated by heparin. The primary side effect is bleeding or hemorrhage.

Streptokinase. Streptokinase is a single-chain protein containing 415 amino acids, mol wt of 45,000 to 50,000 (261,284–286). It is produced by β-hemolytic streptococci and is not an enzyme *per se*. Only after streptokinase combines with plasminogen on a 1:1 basis to form a streptokinase–plasminogen complex, to expose the active site of the plasminogen portion, does it become an active species. This complex then becomes a potent enzyme activator and converts plasminogen to plasmin. The complex has a half-life of about 23 min in the circulation. The usual dose used is 1.5 million units to ensure enough streptokinase is left after being neutralized by streptokinase antibodies and inhibitors in the blood stream. Thrombolytic activity lasts for 3 to 4 h. Streptokinase administration also causes fibrinolysis and fibrinogenolysis, through activation of plasma plasminogen, in the circulation and depletes plasma fibrinogen.

The mortality is usually reduced from 12% in the control group to 9–10% in the streptokinase group. Side effects are bleeding and hemorrhage, fever, and in rare occasions, anaphylaxis.

Urokinase. Urokinase is a direct plasminogen activator that is produced in the kidney and endothelial cells (259,261,263,264,266). It was first isolated from human urine, but now it is produced by cultured human fetal kidney cells. It is a double chain of 411 amino acids, mol wt 54,000–57,000, having a half-life of 16 min. It is metabolized in the liver. Urokinase is given at 4500 units per kilogram in a loading dose and then at 4500 units per kilogram per hour by a continuous iv infusion. Urokinase converts plasminogen to plasmin with greater affinity for the fibrin-bound plasminogen. However, during therapy of AMI, the circulating plasminogen is also activated which catalyzes the breakdown of fibrin and also fibrinogen, causing a generalized (systemic) lytic state. Hemorrhage is the most serious side effect.

Acylated (Anisolyated) Plasminogen–Streptokinase Activator Complex (APSAC). After intravenous administration streptokinase becomes active only after forming a complex with plasminogen. This activated form is rapidly inactivated in the plasma and also causes generalized (systemic) fibrinogenolysis. Therefore, most of the active complex cannot reach the arterial thrombus in the coronary circulation. To overcome this, the active site (catalytic center) of the preformed streptokinase–plasminogen complex is protected or blocked by an acyl group and APSAC is formed (259,261,263,264,266,287–289). However, the fibrin-binding sites are not changed, therefore APSAC binds rapidly to the fibrin clot. So the local dissolution of the clot is preferentially obtained. Deacylation occurs slowly in plasma.

In acylated form, the APSAC offers a prolonged half-life (105 min), greater lysis potency, and less systemic lytic state. APSAC is used at 30 U (30 mg) by iv injection.

Prourokinase. The single-chain urokinase-type plasminogen activator (scu-PA) urokinase does not have high fibrin specificity and therefore causes systemic fibrinogenolysis. In the early 1980s, a single-chain precursor of urokinase (prourokinase) was isolated and purified in human urine and cultured cell lines. It is produced using recombinant DNA biotechnology techniques. It was found that prourokinase was much more fibrin-specific than urokinase and is not effective in activating plasma plasminogen. Its mechanism of action was distinctly different from that of t-PA.

Prourokinase is a single-chain protein containing 411 amino acids (261,265,274,275). In clinical uses scu-PA does not bind to fibrin only and its use causes a decreased plasma fibrinogen of 80%. Its half-life in the circulation is 5 min. It is cleared by the liver. It is used at 40–70 mg over 1 h and heparin is needed simultaneously. Fibrin specificity and thrombolytic efficacy are similar to that of t-PA.

ECONOMIC ASPECTS

The cardiovascular agents are the fastest growing segment of the world pharmaceutical market. In 1990, the world ethical pharmaceutical market was \$77.5 billion. The overall growth rate between 1978–1988 was 18% per annum but was expected to slow 10% per annum between 1988–1993. Despite the projected slowing of the total market, cardiovascular agents are expected to continue to make substantial progress in all world markets. Estimated worldwide sales of cardiovascular agents for 1993 are greater than \$38 billion. U.S. sales alone are expected to be in excess of \$10 billion. The estimated 1993 worldwide sales of cardiovascular agents for the treatment of specific cardiovascular diseases are summarized in Table 8 (290,291).

Table 8. 1993 Worldwide Sales of Cardiovascular (CV) Agents^a

Therapeutic area	Sales, \$ × 10 ⁹	CV market share, %
hypertension	~12.6	34.6

angina	~5.2	14.1
congestive heart failure	~6.2	17.0
other cardiovascular diseases, eg, arrhythmias	~12.1	33.0

^a Estimated.

The projected 1993 U.S. sales of various classes of cardiovascular agents are summarized in Table 9 (290,291). Estimates for worldwide sales of antihypertensives alone in 1992 are approximately \$10 billion. Thus the number of cardiovascular agents in development is numerous, eg, >45 antiarrhythmics; however, the probability of many becoming therapeutic agents is extremely small.

Table 9. 1993 U.S. Sales of Cardiovascular (CV) Agents of Various Classes of Cardiovascular Agents^a

Class of CV agent	Sales, \$ × 10 ⁶ ^a
antihypertensives	~6.2
antiatherosclerotics	~1.8
thrombolytics	~0.6
nitrates, antiplatelet agents	~0.7
antiarrhythmics	~0.4
other agents	~0.5

^a Estimated.

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CARNALLITE.

See POTASSIUM COMPOUNDS.

CARNAUBA WAX.

See WAXES.

CARNOTITE.

See URANIUM AND URANIUM COMPOUNDS.

CAROTENOIDS.

See VITAMINS, VITAMIN A.

CASEHARDENING.

See METAL SURFACE TREATMENTS.

CASEIN.

See MILK AND MILK PRODUCTS.

CASTOR OIL

Castor oil [8001-79-4] is derived from the bean of the castor plant *Ricinus communis*, belonging to the family Euphorbiaceae. The castor bean is not a legume as the name implies but is a member of the spurge family. Castor plants occur in practically all tropical and subtropical countries. They are also grown annually from seed as both ornamental and cultivated plants in temperate zones. There are wide variations in the size, form, and color of the plant, as well as the size and color of the seed. Colors vary from extreme red to pure green and the stems, leaves, and fruits are covered to a varying extent by a waxy, bluish bloom. The usually three-seeded capsules may be spiny and display great variety in size, shape, and color patterns. There is, however, relatively little variation in the oil content of the fully matured seeds and in the chemical composition of the oil derived therefrom (1,2).

The seeds of the castor plant are produced in racemes, or clusters of capsules. The capsules each contain three seeds protected by a hull that is removed prior to processing. The seeds are mottled to varying extents, most often with shades of dark brown overlaying shades of light brown. Seeds of commercial varieties range from 250 to 1800 kg. The seeds are toxic, and the ingestion of several seeds can be fatal to humans.

Whereas commercial production of castor oil existed in the United States in the 1800s, production shifted to tropical and subtropical countries in the early 1900s. World War I, World War II, and the Korean conflict each influenced efforts to produce hybrid castor species and increase U.S. planting, and by the late 1960s, approximately 80,000 acres of castor were grown in the United States producing 29,500 metric tons of castor oil. U.S. production was competitive until 1972 when Federal price supports were withdrawn. U.S. production dropped almost to zero by 1974.

Interest in the restoration of U.S. castor seed production was initiated in 1989. An aggressive hybrid seed program was developed in Texas (3), and sufficient hybrid seed was grown in 1990 to plant 40,000 acres of castor in 1991. Mechanization of harvesting equipment for the collection of dwarf (~1 m) hybrid plants retaining the seed pods on the plant until harvested, was expected to yield from 800–900 kilograms of seed per acre. Although the U.S. Department of Defense continues to classify castor derivatives as a critical strategic material, in 1990, the United States imported 100% of its castor oil needs primarily from Brazil and India. Furthermore, fluctuating supplies and prices of imported oil fostered the use of alternative feedstocks (see CHEMURGY).

Properties

Castor oil is also known as ricinus oil, oil of Palma Christi, tangantangan oil, and neoloid. Typical of vegetable oils and most fats, castor oil is a triglyceride of various fatty acids (see FATS AND FATTY ACIDS.) Its uniqueness stems from the very high (87–90 wt %) content of ricinoleic acid, C₁₈H₃₄O₃, structurally *cis*-12-hydroxyoctadeca-9-enoic acid, CH₃(CH₂)₅CH(OH)CH₂CH=CH(CH₂)₇COOH, an eighteen-carbon hydroxylated fatty acid having one double bond. Castor oil, sometimes described as a triglyceride of ricinoleic acid, is one of the few commercially available glycerides that contains hydroxyl functionality in such a high percentage of one fatty acid.

The average fatty acid composition of castor oil is given in Table 1 (4). Castor oil, is the only significant oil composed mainly of the glyceride of a hydroxylated fatty acid. Ricinoleic acid has an acid value of 180, a saponification value of 186, a Wijs iodine value of 89, and a melting point of 5.5°C. The 12th carbon is asymmetric, resulting in an optical rotation of [α]_D²² = 6.67. Other ricinoleic acid properties are Gardner color 5; viscosity at 25°C, 400 mm² s (cSt); pour point, 23°C; specific gravity at 25°C, 0.940; index of refraction at 25°C, 1.4699. Ricinoleic acid cannot be distilled unless special precautions are taken via derivative formation to protect the hydroxyl group.

Table 1. Fatty Acid Composition of Castor Oil

Fatty acid	CAS Registry number	Molecular formula	Wt % ^a
ricinoleic acid	[141-22-0]	C ₁₈ H ₃₄ O ₃	89.5
dihydroxystearic acid	[26248-43-1]	C ₁₈ H ₃₄ O ₄	0.7
palmitic acid	[57-10-3]	C ₁₆ H ₃₂ O ₂	1.0
stearic acid	[57-11-4]	C ₁₈ H ₃₆ O ₂	1.0
oleic acid	[112-80-1]	C ₁₈ H ₃₄ O ₂	3.0
linoleic acid	[60-33-3]	C ₁₈ H ₃₂ O ₂	4.2
linolenic acid	[436-40-1]	C ₁₈ H ₃₀ O ₂	0.3
eicosanoic acid	[506-30-9]	C ₂₀ H ₄₀ O ₂	0.3

^a These are typical values.

Standards for industrial quality castor oil as specified by the ASTM are given in Table 2, and other general properties of castor oil are listed in Table 3.

Table 2. Industrial Castor Oil Standards^a

Property	Value
acid value, max	2.0
clarity	clear
Gardner color, max	2
hydroxyl value	160–168
loss on heating, wt % max	0.2
refractive index, 25°C	1.4764–1.4778
saponification value	176–184
solubility in alcohol ^b	complete
specific gravity, 25–25°C	0.957–0.961
unsaponifiable matter, wt % max	0.7
viscosity, mm ² s (cSt)	6.50–8.00
iodine value	84–88

^a Ref. 5.

^b Soluble 1:2 by vol in 95% ethanol at 20°C.

Table 3. Properties of Castor Oil

Property	Value
viscosity, ^a 25°C, mm ² s (cSt)	615–790
flash point, Cleveland open cup, °C	285
tag closed cup	230
surface tension, mN/m	39.0
20°C	39.0
80°C	35.2
Reichert-Meissl value	<0.5
Polenske value	<0.5
acetyl value	144–150
optical rotation (polarimeter, 200 mm)	+7.5–9.0
pour point, °C	23
coefficient of expansion, mL/°C	0.00066

^a Value corresponds to $U \pm \frac{1}{2}$ in Gardner-Holdt units (see RHEOLOGICAL MEASUREMENTS).

Castor oil is distinguished from other triglycerides by its high specific gravity, viscosity, and hydroxyl value. Another unique feature is alcohol solubility: one volume of castor oil dissolves in two volumes of 95% ethyl alcohol at room temperature, and the oil is miscible in all proportions with absolute ethyl alcohol. Also the oil is typically soluble in polar organic solvents and less soluble in aliphatic hydrocarbon and other nonpolar organic solvents. Its slight solubility in petroleum ether is a characteristic distinguishing it from other fats. The oil can vary in color depending on the method of recovery and blending to meet specifications. Normally, it is pale yellow, highly viscous, and has a slight characteristic odor. Although it is nearly tasteless, its minor use as a cathartic agent has earned it an unenviable reputation.

Quality and Specifications

The quality of various grades of castor oil have been prescribed by the International Castor Oil Association, Inc. (ICOAI). Specifications prescribed for the triglyceride oil derived from a plant of the genus *Ricinus communis* are shown in Table 4. The International Castor Oil Association, Inc. has also established chemical properties to be used in the event of a dispute between buyer and seller as to the purity of the oil. These specifications are given in Table 5.

Table 4. Castor Oil Quality and Specifications^a

Property	Pale oil	No. 1 oil	No. 2 oil	No. 3 oil
color, AOCS ^{b,c} tintometer,	10 yellow–1.0 red	20Y–2.0R	30Y–3.0R	40Y–4.0R

free fatty acids, ^c wt %	0.75	1.00	1.50	3.0
acid value, ^c	1.49	1.99	2.98	5.97
moisture and volatiles, ^c wt %	0.255	0.355	0.485	0.485
water content, ^c (Karl Fischer), wt %	0.25	0.35	0.48	0.48
insoluble impurities, ^c wt %	0.01	0.02	0.02	0.2
appearance, 25°C	brilliantly clear; free of suspended matter	characteristically clear; free from suspended matter	characteristically clear; and free from suspended matter	not exceeding slight haze; free of suspended matter
odor	very slight; characteristic	slight; characteristic	slight; characteristic	characteristic

^a All oil has viscosity in the 680–900 mm² s (cSt) range, equivalent to a U-V classification in Gardner-Holdt units.

^b AOCS American Oil Chemists Society.

^c Values given are maximum allowable.

Table 5. Commercial Castor Oil Specifications

Property	Pale pressed and No. 1 oils	No. 2 and No. 3 oils	AOCS test method ^a
specific gravity, at 25°C	0.955–0.965	0.950–0.965	Cc 10–25
refractive index at 25°C, <i>n</i> _D	1.476–1.479	1.475–1.480	Cc 7–25
acetyl value, ^b	142	140	Cd 4–40
iodine value	82–88	80–88	Cd 1–25
saponification value	176–184	174–184	Cd 3–25
unsaponifiable matter, ^c wt %	0.7	0.8	Ca 6a–40

^a AOCS American Oil Chemists Society.

^b Minimum value given.

^c Maximum value given.

Oil and Meal Recovery

The commercial process for castor oil recovery from the seed consists of preheating the seed in stack cookers prior to crushing in a hydraulic press or a continuous mechanical screw-type press commonly known as an expeller. The presscake discharged from this mechanical processing contains 10–20 wt % oil and is then processed in solvent extraction units to recover the residual oil. Cold-pressing of castor seed that has not been preheated is still carried out to a limited degree in castor growing countries such as Brazil and India. A light colored, high quality medicinal type oil is recovered. Castor oil recovered from hydraulic or continuous mechanical screw presses requires refining to remove toxic proteins, gums, and foreign matter while improving the color and reducing the free fatty acid content.

Solvent extraction in batch or continuous systems is used to recover most of the residual oil from the presscake. Heptane, hexane, or a mixture of these solvents is used to recover the oil. The solvent-extracted presscake is steam stripped to recover solvent and a residual meal known as castor pomace, containing 1% residual oil. The solvent extracted oil is also processed for solvent recovery (qv). The oil from the extraction procedure is darker than the mechanically pressed oil and has a higher free fatty acid content. It is sometimes referred to as a No. 3 castor oil and is used for blending with higher quality oils that are well above No. 1 specifications.

The castor pomace has a protein content of approximately 35 wt % and is used predominantly as an organic fertilizer for slow release of nitrogen. It has not been used extensively as an animal feed supplement because of the presence of toxins and allergens (6,7). Castor pomace typically analyzes as: 48 wt % carbohydrate, 36 wt % protein, 9 wt % moisture and volatile material, 6 wt % ash, and 1 wt % oil. The castor protein contains a poisonous, but heat labile protein called ricin and a toxic alkaloid known as ricinine and must be further processed. The ricin, present in relatively large amounts, can be easily destroyed by steam heat used in evaporating solvent from the extracted meal. The ricinine, present in small amounts, is not considered significantly detrimental (8). Of primary concern, however, is the presence of a very potent and heat-resistant allergen known as CB-1A. Allergen levels as high as 7 to 12.5 wt % have been recorded for castor; usual levels are 0.7 to 1.5 wt % in the meal before treatment (9–14).

A castor meal treating program for simultaneous detoxification and deallergenation led to the development of a process to detoxify the meal by heat and moisture and to deallergenate by chemical and water treatment utilizing expander extruder processing techniques (14). This detoxified and deallergenated castor meal is safe to use as feed for animals (see FEEDS AND FEED ADDITIVES).

A commercial plant in Thailand successfully treats castor meal at a rate of 3 t/h. The typical amino acid wt % analysis of castor pomace important for livestock rations is methionine 1.5%; threonine, 3.6%; valine, 6.6%; leucine and isoleucine, 12.5%; phenylalanine, 4.2%; tyrosine, 3.2%; proline, 3.9%, aspartic acid, 4.6%; glutamic acid, 18.0%; tryptophane, 0.8%; arginine, 16.0%; lysine, 3.1%; histidine, 2.5%; and other nitrogen compounds, 19.5%. Spectrographic analysis of castor pomace yields wt % values of Ca, 0.35; Mg, 1.17; S, 0.34; Mn, 0.012; Fe, 0.22; Cu, 0.007; B, 0.004; Zn, 0.005; and Mo, 0.0003. Wet analysis shows 1.65 wt % phosphoric acid, P₂O₅ total, and 1.10 wt % water-soluble potash, K₂O. This detoxified, deallergenated meal produced in Thailand is undergoing animal-feed testing. Treated castor meal produced in Texas during 1960–1970 was successfully used in cattle rations. The sales of treated castor meal for animal feeding are expected to play a significant role in stabilizing the price of castor oil.

The recovery of oil to meet specifications of the ICOAI for better quality oils requires four processes:

Degumming. The oil and dissolved and dispersed proteinaceous materials are treated with 3–5 wt % water at a temperature of 70–80°C and passed through a decanter-type centrifuge to separate the gums from solution. Decanter-type centrifuges are virtually a necessity for this operation and a combination of a dry degumming agent and a solids handling decanter offer the most effective first-stage processing of the oil.

Removal of Free Fatty Acids. Alkali treatment of the oil is accomplished by the use of caustic soda solutions to neutralize the excess free fatty acids. Because castor oil readily forms emulsions with water and/or alkaline solutions, special techniques have been developed to neutralize the acids. A continuous counter-current process was developed using a stationary contact reactor (15). Treatment in the presence of a solvent is also utilized (16).

Deodorization. Volatile components present from the processing of castor seed to recover the oil are removed by nitrogen or steam stripping operations. Typical steam stripping is carried out at 160°C under less than 1.5 kPa (11 mm Hg) pressure. Processes have been developed for efficient steam–oil contact (17). A unique method of contacting the oil and steam using closely spaced plates to form vertical channels arranged in sequence has been developed. The sparge steam is injected at the base of the channel, and its expansion, as it leaves the sparge holes, throws the hot oil onto the plates as a film. The oil film is dragged to the top of the plate and to the base of the next channel where the process is repeated with fresh steam injections. The steam and stripped volatiles continue up and out of the stripping zone while the turbulent flow regime in the oil phase overcomes the liquid-phase diffusion of the volatile materials. This thin-film steam stripper exposes the oil to high temperatures for a minimum time span of approximately 20 minutes. Steam refining of

The dehydrated castor oil fatty acids [61789-45-5] are obtained by hydrolysis or by saponification followed by acidification of the dehydrated oil. The conjugated acid content of the product remains the same as in the oil itself. Much higher, 50 wt % and above, conjugated acid contents are obtained by dehydration of ricinoleic acid (31). Usually, the crude acids are distilled under vacuum to obtain a light colored, high quality product. Properties of dehydrated castor acids are shown in Table 7. Type I is distilled grade; Type II is crude, undistilled grade acid.

Table 7. ASTM Requirements for Dehydrated Castor Acids^a

Requirement	Type I	Type II	ASTM method
acid value	195–200	187–195	D1980
saponification value	195–200	193–199	D1962
iodine value	150–156	138–143	D1959
color (Gardner)	1 max	5–8	D1544
spectrophotometric diene value	28–35	25–32	D1358

^a Ref. 32.

Sulfation. Sulfated castor oil, also known as turkey-red oil, represents one of the earliest chemical derivatives of castor oil. The traditional method of preparing turkey-red oil is to add concentrated sulfuric acid at a controlled rate to castor oil over a period of several hours with constant cooling and agitation of the reaction mass to maintain a temperature of 25–30°C. After acid addition is complete, the reaction mass is washed then neutralized using an alkali solution or an amine.

Castor oil sulfation results largely in a sulfuric acid ester in which the hydroxyl group of ricinoleic acid has been esterified. However, other reactions can also take place. For example, the double bond can be attacked to produce an ester or the hydroxysulfonic acid (33). Hydrolysis of the sulfuric acid esters occurs during the reaction and subsequent treatment forming hydroxy acids and sulfuric acid. These hydroxy acids can be further sulfated.

Despite the many reactions and complex mixture obtained by the sulfuric acid treatment, most commercial products seem to be similar in properties (34). Commercially sulfated castor oil contains ca 8.0–8.5 wt % combined SO₃, indicating that the surfactant properties result from the sulfation of only one of the reactive points in the unmodified triglyceride. The sulfate group acts as a hydrophile imparting excellent wetting, emulsification, and dispersing characteristics to the oil. The anion-active product is used in the textile industry for fiber wetting ability and as dye agent to obtain bright, clear colors (35) (see DYES AND DYE INTERMEDIATES; TEXTILES).

Sulfonation of castor oil using anhydrous SO₃ yields a product having better hydrolytic stability than that from the sulfuric acid reaction. The organically combined SO₃ is low compared to the amount of SO₃ introduced to the reaction: the final product contains only 8.0–8.5 wt % combined SO₃ although 17 wt % SO₃ is added. The product contains less inorganic salts and free fatty acids than the sulfuric acid product (36).

Alkali Fusion. The alkali fusion of castor oil using sodium or potassium hydroxide in the presence of catalysts to split the ricinoleate molecule, results in two different products depending on reaction conditions (37,38). At lower (180–200°C) reaction temperatures using one mole of alkali, methylhexyl ketone and 10-hydroxydecanoic acid are prepared. The 10-hydroxydecanoic acid is formed in good yield when either castor oil or methyl ricinoleate [141-24-2] is fused in the presence of a high boiling unhindered primary or secondary alcohol such as 1- or 2-octanol. An increase to two moles of alkali mole ricinoleate and a temperature of 250–275°C produces capryl alcohol [123-96-6], C₈H₁₈O, and sebacic acid [111-20-6], C₁₀H₁₈O₄, (39–41). Sebacic acid is used in the manufacture of nylon-6,10.

Production of Nylon-11. Nylon-11, which accounts for the world's largest single use of castor oil, has unique stability and solvent-resistant properties. Its preparation is based on the steam cracking pyrolysis of methyl ricinoleate (42) produced from the reaction of castor oil and methyl alcohol. Pyrolysis of methyl ricinoleate at ca 450–500°C yields methyl 10-undecylenate and heptaldehyde [111-71-7], C₇H₁₄O. Hydrolysis gives 10-undecylenic acid [112-38-9], C₁₁H₂₀O₂, which upon addition of HBr in the presence of peroxides forms 11-bromoundecanoic acid. This acid reacts with ammonia to form aminoundecanoic acid, known as rilsan monomer (43). Heating of the molten monomer gives the nylon-11 polymer (see POLYAMIDES; FIBERS, POLYAMIDES).

Nylon-11, mp of ca 186–190°C facilitating high speed uniform processing, has the advantage of having a cold impact, no rupture temperature of 40 to 50°C, low moisture sensitivity, and very high zinc chloride resistance. Excellent chemical resistance and stability in contact with all types of fuels, along with vibration and shock resistance, have led to the use of nylon-11 in the automotive industry, as a covering for braided cable, and in industrial fabrics. A variety of bearing and rollers in conveyor systems are fabricated from this material.

The use of nylon-11 for powder coatings or dry coatings (qv) has been developed in response to a growing concern for the environment (44) (see COATING PROCESSES, POWDER TECHNOLOGY). Electrostatic deposition allows thin films to be applied to metal substrates. Once the powder is applied, it must be melted and coalesced into a continuous plastic film. Forced draft or irradiant ovens are used for fusion, and because no polymerization or cross-linkage are required for curing, coated objects can be processed quickly and air-cooled (45).

Hydrogenation. Hydrogenation of castor oil must be carried out at relatively low temperature and pressures to preserve the hydroxy group, functional in the preparation of 12-hydroxystearic acid [106-14-9], C₁₈H₃₄O₃, used for the manufacture of automotive and multipurpose greases (see LUBRICATION AND LUBRICANTS). Optimal results are obtained at 130 ± 5°C at a pressure of 1.5–2.0 MPa (15–20 bars) using 0.2 wt % nickel catalyst. Other catalysts and processing parameters may be used to produce unique derivatives. Simple double-bond hydrogenation at 140°C in the presence of Raney nickel catalyst produces glyceryl tris(12-hydroxystearate) [139-44-6], C₅₇H₁₁₀O₉, having a melting point of 86°C (46,47).

Approximately 40,000–45,000 metric tons of hydrogenated castor oil and 12-hydroxystearic acid are produced annually, accounting for about 10% of the world castor oil production. The hydrogenated castor oil and 12-hydroxystearic acid are used primarily for the manufacture of lubricating greases in the form of lithium soaps. Petroleum-derived base stock containing approximately 8% lithium soap is used as an automotive grease. Special high viscosity greases contain 20–30% of the lithium 12-hydroxystearic soap. The needlelike structure of the soaps impart better stability and lubricity to greases that are impervious to water. They perform better than tallow stearate containing greases (48).

Conversion of castor oil or the methyl ester to the fatty alcohol can be accomplished by sodium reduction or high pressure hydrogenation. Quantitative reduction to ricinoleyl alcohol [540-11-4], C₁₈H₃₄O₂, is achieved using a secondary reducing alcohol in the presence of sodium suspensions in refluxing xylene. Hydrogenation of ricinoleic acid using a copper–cadmium catalyst at 220°C and 26 MPa yields 70% ricinoleyl alcohol (49).

The preparation of methyl 12-ketostearate from methyl ricinoleate has been accomplished using copper chromite catalyst. The ketostearate can also be prepared from methyl ricinoleate in a two-step process using Raney nickel. The first step is a rapid hydrogenation to methyl 12-hydroxystearate, the hydrogen coming from the catalyst, followed by a slower dehydrogenation to product (50,51).

Partial hydrogenation of castor oil results in waxes (qv) of modified chemical properties when hardness, flexibility, melting point, and iodine value of the products are controlled by degree of hydrogenation. Castor oil esters are changed by hydrogenation from fluid products to soft waxes having mp of 45–80°C. These products are used in antiperspirants (see COSMETICS), leather (qv) coatings requiring oil resistance and water imperviousness, and in roll leaf foils because of their alcohol solubility and excellent wetting adhesion to metallic particles.

Pyrolytic Decomposition. The pyrolytic decomposition at 350–460°C of castor oil or the methyl ester of ricinoleic acid splits the ricinoleate molecule at the hydroxyl group forming heptaldehyde and undecylenic acids. Heptaldehyde, used in the manufacture of synthetic flavors and fragrances (see FLAVORS AND SPICES; PERFUMES) may also be converted to heptanoic acid by various oxidation techniques and to heptyl alcohol by catalytic hydrogenation. When heptaldehyde reacts with benzaldehyde, amyl cinnamic aldehyde is produced (see CINNAMIC ACID, CINNAMALDEHYDE, AND CINNAMYL

ALCOHOL). Undecylenic acid, the nylon-11 precursor, is also used for its fungicidal and bactericidal properties. A combination of undecylenic acid and zinc undecylenate [557-08-4] is used in the treatment of athlete's foot infections. The copper salt has been compounded into ointments used in treating facial and body infections (52) (see ANTIPARASITIC AGENTS).

Alkoxylation. Alkylene oxides react with the hydroxyl groups of castor oil to yield an infinite variety of polyoxyalkylene derivatives. The reaction at 120–180°C and 0–415 kPa (0–60 psi) uses alkaline catalysts such as sodium hydroxide. Free-radical-type acid catalysts are also used at lower temperature and pressure (53). The most important group of products, the ethoxylated derivatives, are nonionic surface-active agents having various degrees of hydrophobic–hydrophilic properties. The low level ethoxylated derivatives are water emulsifiable and used as defoamers (qv) and de-emulsifiers for petroleum emulsions. The highly ethoxylated products are water-soluble and excellent solubilizers for water-insoluble oils in cosmetic compositions (54–56). They are also used as components in detergents, lubricating and cutting oils, hydraulic fluids (qv) (57), textile finishing compositions, and as antistatic agents (qv) for nylon carpets and apparel (58,59). The propoxylated derivatives are mineral oil-soluble and useful in lubricating oils and hydraulic fluid compositions. Approximately 6500 metric tons of ethoxylated castor oil were produced in the United States in 1988.

Oxidation. Oxidized or blown castor oils are clear viscous oils that are made by the intimate mixing (blowing) of castor oil and air or oxygen at 80–130°C, with or without the use of a catalyst. The reaction is a combination of oxidation and polymerization promoted by transitional metals like iron, copper, and manganese (60,61). The range of the properties of commercially available oils are given in Table 8.

Table 8. Properties of Oxidized Castor Oils

Property	Value
color (Gardner) ^a	2–13
viscosity at 25°C, mm ² s(cSt)	1,100–200,000
specific gravity at 25°C	0.970–1.028
acid value	5–25
saponification value	188–225
iodine value	80–50
hydroxyl value	160–125

^a Color ranges from pale to dark brown.

Oxidized castor oils are excellent nonmigrating, nonvolatile plasticizers (qv) for cellulosic resins, poly(vinyl butyral), polyamides, shellac, and natural and synthetic rubber (see RUBBER, NATURAL). The high viscosity products are also used as tackifiers in gasket compounds and adhesives (qv) because of good oil and solvent resistance. They also serve as excellent pigment grinding media and as a base for inks (qv), lubricating oils, and hydraulic oils (62).

Economic Aspects

Whereas castor oil is available on a worldwide basis from many sources, India, Brazil, and China produced nearly 80% of the world's castor seed for the period 1986–1989 (63) as seen in Table 9. In the small number of significant producing and exporting nations that grow castor, traditional agricultural practices are used, and practically all castor plants are grown under dryland conditions and hand harvested. Much of the castor crop is harvested from small farms that are fully dependent on natural weather conditions, contributing to fluctuations in both supply and price. Yield of castor seed per acre is reported at 270–450 kilograms per acre.

Table 9. World Production and Trade of Castor Oil, t/yr (1986–1989)

Country	Production ^a	Exports ^b	Imports ^b
Brazil	100,350	79,852	
India	85,750	39,667	
China	65,341	26,495	
Russia ^c	26,525		357,000
Germany ^d	17,000	5,430	10,988
Japan	15,416	181	
Thailand	15,313	8,950	
United States			36,850
France			41,781
United Kingdom			8,420
Poland			4,695
The Netherlands			3,776
Total	359,839	167,558	167,972

^a Ref. 63.

^b Ref. 64.

^c Figures are for the former USSR.

^d Figures are for the former FDR (West Germany).

Wholesale prices for No. 1 castor oil in tank car lots was \$1.11 /kg in 1990 compared to \$1.60 /kg in 1984 and \$0.74 /kg in 1986 (65). Brazil, China, and India accounted for about 85% of the world exports, and France, the United States, Russia, Germany, and the United Kingdom accounted for about 75% of the world imports from 1986–1989.

A more reliable castor oil supply is being sought through genetic efforts. In 1985, a project was established in Costa Rica for the production of hybrid castor seeds to improve the oil content of the seed, make the seed totally nondehiscent, ie, prevent the seed from breaking out of the capsule and falling to the ground as it ripens allowing for mechanical harvesting (66). The European Community (EC) lists castor production as the number one demonstration priority, and the Costa Rican technology has been utilized in France where hybrid castor seed for mechanical harvesting was planted in 1990. A project was also initiated in the United States in 1989 to revive domestic production of castor seed on the high plains of Texas (67). A hybrid castor seed (H-22), developed by the Weizman Institute in Israel, is most widely used by underdeveloped countries where crops are hand harvested. New dwarf varieties are being developed for mechanical harvesting (68).

Applications

Castor is the only renewable vegetable oil resource (see CHEMURGY) having a hydroxyl group structure and functionality that leads to diverse oleochemicals. In 1988, approximately 35,000 t /yr of castor oil were used to prepare raw materials for the manufacture of nylon-11. It is estimated that 40,000–45,000 t of

oil are used annually to manufacture hydrogenated castor oil waxes and 12-hydroxystearic acid for automotive greases. In 1989, the United States used 15,000 t of castor oil to manufacture sebacic acid and ethoxylated castor oils, and India used 35,000 t of oil for the manufacture of raw materials used in surface coatings (69).

Polyamides. Nylon-11, accounts for the largest single use of castor oil. Pyrolysis of the oil yields methyl undecylenate, which is converted to 11-amino-undecanoic acid. Condensation of this monomer produces nylon-11, known commercially as Rilsan 11 (Atochem, Inc.). Nylon-11 is used as an engineering plastic in the automotive and transport industry in the form of fuel lines. Products are also used for extruded and molded components of fuel systems such as filler necks, gas tanks, reservoir modules, filters, fuel rails, and vapor recovery systems. Air brake hoses on large trailer truck transports are made of nylon-11, and nylon-11 tubing is used in the compressed air industry in pneumatic control systems. In addition, nylon-11 is used in powder coatings to coat metals that require abrasion, impact, and corrosion resistance. Nylon-11 offers high dimensional stability, close molding tolerance, high abrasion and impact resistance, excellent dielectric strength, low moisture absorption, electrical insulating properties, and overall chemical resistance and durability (45,70).

Urethanes. Castor oil is used as a reactive component with polyfunctional isocyanates to prepare polyurethane compounds (see URETHANE POLYMERS). Castor oil has been polymerized with toluene diisocyanate (see ISOCYANATES, ORGANIC) and combined with polystyrene phase to produce a semi-interpenetrating polymer network upon heating. This interpenetrating polymer network provides a route for improving brittleness of thermosetting plastics and increasing the morphology and toughness of the final elastomer. Tough plastics were derived based on castor oil-elastomer-reinforced vinyl polymers (qv) and simultaneous interpenetrating networks prepared by cross-linking castor oil with sebacyl chloride and polystyrene (see STYRENE PLASTICS) (71–73). Water-resistant polyurethane-based encapsulants were prepared from castor oil polyols and plasticizers. The cured elastomer is used to encapsulate plastic insulated telephone cables and seal the interior spaces of the electrical connections from the incursion of water (74–77).

Urethane casting resins prepared from castor polyols exhibit a broad range of properties from hard plastics to soft elastomers. These two-component liquid urethanes are reported to have good electrical and mechanical properties, good shock absorption, low exotherm, low shrinkage, and excellent hydrolytic stability and heat aging properties (78–81). These castor-based casting resins are used principally for potting and encapsulation of electrical components.

Low viscosity urethane polymers have been prepared from castor oil and polymeric isocyanates (82). These low mix viscosity systems are extremely useful for potting electrical components where fast penetration without air voids, and fast dispensing cycles are desirable. Very low viscosity urethane systems containing castor polyols have been prepared for use in reclaiming water-logged buried telephone cable and for encapsulating telephone cable splices (83–86).

Polymerization of castor oil, chemical or oxidative, results in higher viscosity or bodied oils that are more useful in urethane coatings than the untreated castor oil (87). Other castor derivatives used to prepare urethanes are amides prepared by reaction of castor oil and alkanolamines, amides of ricinoleic acid with long-chain di- and triamines, and butanediol diricinoleate (88,89).

By varying molecular weight and functionality of the castor polyols and the type of isocyanate, a variety of clear and pigmented urethane coatings can be prepared. Copolymers of vinyl and castor-based urethane have also been reported for use as exterior coatings for plywood and flexible substrates (90) and for application over steel, concrete, and wood substrates (91).

Castor oil and its polyol derivatives have been found to be very useful in the preparation of rigid, semirigid, and flexible urethane foams. Castor oil's resistance to hydrolysis, pigment dispersion ability, and compatibility with polyether polyols has also made it useful as a modifier for polyether-based foam. These foams generally possess an open cell structure (92). Castor oil can also be used to formulate commercially acceptable rigid urethane forms for such uses as thermal insulations and structural support (93). Superior rigid urethane foams have been prepared from hydroxymethylated polyol esters of castor acids (94). Brominated castor oil has been investigated as a modifier for preparing fire-resistant urethane foams (95,96).

Coatings. A variety of castor oil derivatives are utilized in the preparation of surface coatings (qv). Dehydrated castor oil fatty acids (DCOFA) react with phthalic anhydride and other polyols to produce a water-soluble, air-drying alkyd resin (97). Reaction of an acrylamide polymer, combined with styrenated acrylates and an oil modified maleic polyester, is effective in producing appearance finishes, and aluminum coil and metal protective coatings (98). Copolymerization of DCOFA with acrylic esters or reaction of DCOFA with hexamethoxy methylolated melamine resins followed by neutralization with ethyl amine give an aqueous solution useful as a water-soluble resin for an electrodeposition coating (99). Aliphatic polyurethane coating compositions are prepared from trimethylolpropane, dehydrated castor oil fatty acids, 4,4-dicyclohexylmethane diisocyanate, and other components to prepare a weather-resistant finish suitable for use on motor vehicles (100). Coatings from castor oil—toluene diisocyanate copolymers exhibited high abrasion resistance on steel plates and flexibility on aluminum plates and PVC cloth.

A copolymer latex emulsion system utilizing dehydrated castor oil fatty acids yields superior wall paints providing adhesion to varnishes and glossy surfaces (101). Acrylic esters of castor oil are used in solution for the emulsion polymerization coatings process. Water-soluble resins and paints prepared with maleated dehydrated castor oil were used in electrodeposition of water-soluble primers containing 10 to 15% solids for optimum paint film thickness (102). Cathodically electro-depositable binders prepared using dehydrated and maleated dehydrated castor oil fatty acids resulted in binders that gave good adhesion of maximum film thickness (103–105).

Lubricants. Selection of lubricants is based on ability to mitigate wear and friction under the overall conditions of the intended application. Lithium 12-hydroxystearate gives superior thickening and grease forming properties because of the hydroxyl group and helical structure of its crystalline form (106). Sebacic acid, produced by the alkali fusion of castor oil, is the raw material for a series of esters used as nonvolatile, high temperature lubricants for jet engines (107,108). Partially dehydrated castor oils and USP grades of castor oil are approved for trolley lubrication in meat packing plants and extended to applications for lubricants having incidental food contact (109,110).

Sulfated castor oil is incorporated with mineral oil and isopropylamine salts of C₁₂–C₁₈ fatty acids as a lubricant for presizing polyester fibers. The lubricant minimized undesirable abrasion of sizes and facilitated subsequent weaving operations (111). A nontoxic lubricating cutting oil for metals at 700–1200°C is prepared from aluminum powder, graphite, potassium soap, and castor oil (112).

Textiles. Polyamides having improved antistatic properties utilize polyoxyalkylated hydrogenated castor oil as the dispersible antistatic agent (113). A finish for bulked continuous polyamide filament yarns also use polyoxyethylated castor oil to enhance the fiber finish (114).

Different polyamide fibers with varying affinities for anionic dyes are pretreated with aqueous acidic solution containing sulfated castor oil to give uniform shade levels. Sulfated castor oil is also used in compositions for treatment of fabrics, skins, and furs to clean and revive colors (115).

Cosmetics. Castor oil and its derivatives are utilized in cosmetic and personal care products. The low pour point and high viscosity produce lubricity and wetting properties desired in lipsticks. Basic lipstick contains 20–44 wt % castor oil, which also acts as an ideal dispersant for pigments (116). One lipstick formula contains 38 wt % castor oil and 9.5% glycerol monoricinoleate (117).

Castor esters have been found to be nonirritating and noncomedogenic to the skin. Cetyl ricinoleate was found to be an effective noncomedogenic moisturizer (118). Castor-based quaternaries prepared by reaction of a castor fatty acid and a tertiary diamine are used for hair care. The ricinoleic quaternium is incorporated into clear shampoo formulations for foam enhancement and conditioning (119,120).

Hydrogenated castor oils are utilized as a principal ingredient in the manufacture of solid antiperspirant stick formulations. The high melting point of the wax reduces the solidification time in the manufacture of the sticks, resulting in a uniform dispersion of the antiperspirant active ingredients. Hydrogenated castor oils impart emollient and lubricant properties to ointment and cosmetic preparations and act as thixotropic agents in cosmetic gels (118).

Ethoxylated castor oils or ethoxylated castorwaxes are used as solubilizers of hydrophobic substances in cosmetics. Examples are Cremophor EL (ethoxylated castor oil) and Cremophor RH (40–60 ethoxylated hydrogenated castor oil). Other ethoxylated triglycerides are not as effective as castor oil. Ethoxylated castor oil is also a good solubilizer for vitamin A palmitate (121).

Surfactants and Dispersants. Castor oil can be transformed from an oil- to a water-soluble surfactant, depending on the moles of ethylene oxide added to its hydroxyl group. A 40 mole ethylene oxide adduct of castor oil, known as PEG-40 castor oil, is a surfactant that has cosolvent properties and is utilized as a fragrance solubilizer (118). Glycol hydroxystearate emulsifiers are formulated into shampoos to impart finer pearlescence and give better stability than glycol stearates (118) (see HAIR PREPARATION).

Castor oil fatty acid amide polyethylene ethers exhibited dispersant, antimicrobial, emulsifying, and wetting properties. Combining the ethers with

magnesium ricinoleate exhibited rust inhibition on aluminum, iron, and brass (122).

Mixtures containing sulfated castor oil were used to increase the lubricity of water base drilling fluids (123). Sulfated castor oil is also used in dishwashing compounds as a hand softener. A typical cleaning composition contains sodium dodecylbenzene sulfonate, sulfated castor oil, ethanol, and water. A sulfated derivative of castor oil is used as a dispersant for plaster of Paris, reducing the water needed to form a plastic slurry (124). Pesticide emulsions can be stabilized using ethoxylated castor oil (125).

Using sulfated castor oil in the electroplating of zinc results in a good coating, a brilliant plate, and fairly good covering (126). Emulsified noncreosotic pine oil disinfectant compositions have been prepared using <7 wt% of an emulsifier mixture and soaps of castor oil and mixture of soaps of tall oil (127), and a red stamp ink composition, by dispersing pigment particles coated with ethyl cellulose in alkylene oxide modified castor oil (128). A partially saponified castor oil, prepared by reaction of an ethoxylated castor oil and alkali metal hydroxide, resulted in surfactants of excellent detergency, low foaming characteristics, stability in alkali and acid solutions, complete water solubility, and no cloud point in typical aqueous use solutions (129).

Polyoxyethylated castor oil containing 42 moles of ethylene oxide may be used under the Federal Food, Drug, and Cosmetic Act as an emulsifier in nitrocellulose coatings for paper and paperboard intended for use in contact with fatty foods at a maximum level of 8 wt % of the coating solid (130).

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CATALYSIS

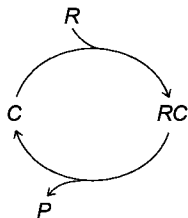
Homogeneous catalysis,
Heterogeneous catalysis,

Catalysis is the key to efficient chemical processing. Most industrial reactions and almost all biological reactions are catalytic. The value of the products made in the United States in processes that at some stage involve catalysis approaches a trillion dollars annually, which is more than the gross national products of all but a few nations of the world. Products made with catalysis include food, clothing, drugs, plastics, detergents, and fuels. Catalysis is central to technologies for environmental protection by conversion of emissions.

This article is an introduction and survey that states the fundamental principles and definitions of catalysis, demonstrates the unity of the subject, and places it in an applied perspective. The selection of industrial catalytic processes discussed has been made for the sake of illustrating principles and representative characteristics of catalysis and catalytic processes. Details of the processes are given in numerous other articles in the *Encyclopedia*.

A catalyst is a substance that increases the rate of approach to equilibrium of a chemical reaction without being substantially consumed itself. A catalyst changes the rate but not the equilibrium of the reaction. This definition is almost the same as that given by Ostwald in 1895. The term catalysis was coined in ca 1835 by Berzelius, who recognized that many seemingly disparate phenomena could be described by a single concept. For example, ferments added in small amounts were known to make possible the conversion of plant materials into alcohol; and there were numerous examples of both decomposition and synthesis reactions that were apparently caused by addition of various liquids or by contact with various solids.

Berzelius attributed catalytic action to ill-defined forces, and the value of Ostwald's more lasting definition is that it identified catalysis as a phenomenon that was consistent with the emerging principles of physical chemistry. Now it is well recognized that catalysts function by forming chemical bonds with one or more reactants, thereby opening up pathways to their conversion into products with regeneration of the catalyst. Catalysis is thus cyclic; reactants bond to one form of the catalyst, products are decoupled from another form, and the initial form is regenerated. The simplest imaginable catalytic cycle is therefore depicted as follows:



where *R* is the reactant, *P* the product, *C* the catalyst, and *RC* an intermediate complex. The intermediate complexes in catalysis are often highly reactive and not observable.

Ideally, the catalyst would cycle forever between *C* and *RC* without being consumed. But in reality there are competing reactions, and catalysts are converted into species that are no longer catalysts. In practice, catalysts must be regenerated and replaced. Catalyst manufacture is a large industry; catalysts worth some \$2–3 billion are sold annually in the United States.

Catalysts may be gases, liquids, or solids. Most catalysts used in technology are either liquids or surfaces of solids. Catalysis occurring in a single gas or liquid phase is referred to as homogeneous catalysis (or molecular catalysis) because of the uniformity of the phase in which it occurs. Catalysis occurring in a multiphase mixture such as a gas–solid mixture is referred to as heterogeneous catalysis; usually this is surface catalysis. Biological catalysts are proteins, ie, poly(amino acids), called enzymes. Some enzymes are present in cytoplasmic solution in cells and others are anchored in cell membranes or on surfaces. Traditionally, homogeneous catalysis, heterogeneous catalysis, and enzymic catalysis have been regarded as almost separate disciplines, and the language and literature have developed without much coherence and overlap.

The performance of a catalyst is measured largely by criteria of chemical kinetics, as a catalyst influences the rate and not the equilibrium of a reaction. The catalytic activity is a property of a catalyst that measures how fast a catalytic reaction takes place and may be defined as the rate of the catalytic reaction, a rate constant, or a conversion or temperature required for a particular reaction under specified conditions. The selectivity is a measure of the property of a catalyst to direct a reaction to particular products. There is no single definition of selectivity, but it is sometimes defined as a ratio of activities, such as the ratio of the rate of a desired reaction to the sum of the rates of all the reactions that deplete the reactants. Selectivity may also be represented simply as a product distribution. Because catalysts lose activity and selectivity during operation, they are also evaluated in terms of stability. The stability of a catalyst is a measure of the rate of loss of activity or selectivity. In practical terms the stability might be measured as a rate of deactivation, such as the rate of change of the rate of the desired catalytic reaction or as the rate at which the temperature of the catalyst would have to be raised to compensate for the activity loss. Catalysts that have lost activity are often treated to bring back the activity, ie, reactivated; the regenerability is a measure, often not precisely defined, of how well the activity can be brought back. Technological catalysts are also evaluated in terms of cost; in a typical process, the cost of the catalyst is a small fraction of the total processing cost, often only a few cents or less per kilogram of product.

Liquid-phase catalysts are used in batch and flow reactors. Batch reactors are predominant in small-scale operations and those designed for flexibility such as pharmaceutical and fine chemicals manufacture. Flow reactors predominate in large-scale processes such as commodity chemicals manufacture and petroleum refining. Corrosion, separation, and catalyst recovery and recycle are usually important issues in these processes. Solid catalysts are used in batch and flow reactors; in most large-scale operations, solid particles of catalyst are present in fixed- or fluidized-bed reactors with gaseous or liquid reactants flowing through them (see REACTOR TECHNOLOGY).

The solids used as catalysts are typically robust porous materials with high internal surface areas, typically, hundreds of square meters per gram. Reaction occurs on the internal catalyst surface. The typical solid catalyst used in industry is a composite material with numerous components and a complex structure.

Catalytic processes are classified roughly according to the nature of the product and the industry of application, and to some degree separate literatures have developed. In chemicals manufacture, catalysis is used to make heavy chemicals, eg, ammonia and sulfuric acid; commodity chemicals, eg, acetic acid and *n*-butyraldehyde; and fine chemicals, eg, fragrances and flavorings. Catalysis is used extensively in the manufacture of pharmaceuticals. In fuels processing, catalysis is used in almost all the processes of petroleum refining and in coal conversion and related synthesis gas (CO and H₂)

conversion. Most of the recent large-scale developments in industrial catalysis have been motivated by the need for environmental protection. Many processes for abatement of emissions are catalytic; automobile exhaust conversion catalysts are now the most important of all in terms of sales volume, and catalysts for conversion of nitrogen oxides in stationary power plant effluents are used on a massive scale in Japan and parts of Europe. Most of the applications of catalysis in biotechnology (qv) are fermentations, often carried out in stirred reactors with gases, liquids, and solids present; the catalysts are enzymes present in living organisms such as yeasts. There are recent applications of whole biological cells and of individual enzymes mounted on supports, ie, carriers, and used in fixed-bed reactors (see ENZYMES, INDUSTRIAL APPLICATIONS).

History

The science of catalysis is driven by technology, as it has been from the beginning. Some of the earliest known examples of controlled chemical transformations are catalytic. Fermentation (qv) was used in ancient times to make alcoholic beverages, and a number of the earliest examples of chemical technology were also exploitations of catalysis (1). For example, before the sixteenth century ether was made by distilling spirits in the presence of sulfuric acid. In 1746 nitric oxide was used as a catalyst in the lead chamber process for oxidation of sulfur dioxide to give sulfur trioxide in the manufacture of sulfuric acid. In 1781, acids were used to catalyze the conversion of starch into sugar. In 1817 H. Davy discovered that in the presence of platinum, mine gases were oxidized at low temperatures; he designed a safety lamp for miners in which the platinum glowed if the flame was extinguished (2). Many more practical discoveries were made in the 1800s (1,2).

These examples existed prior to Ostwald's definition (1), ie, before the nature of catalysis was well understood. But in 1850 Wilhelmy (3) made the first measurements of kinetics of catalytic reactions in an investigation of sugar inversion catalyzed by mineral acids. In the years following Ostwald's definition, just as the principles of chemical equilibrium and kinetics were becoming known, the field of catalysis became more quantitative and developed rapidly. Kinetics of surface catalyzed reactions were measured by Bodenstein (4) just after the turn of the century. The defining work that set the stage for modern catalytic technology was the development of the ammonia (qv) synthesis process by Haber, Bosch, Mittasch, and co-workers at BASF in Germany, beginning ca 1908 (1,5).

Haber and co-workers worked out methods of catalyst testing and process development that are essentially the methods of choice today (6,7). These pioneers understood the interplay between chemical equilibrium and reaction kinetics; indeed, Haber's research, motivated by the development of a commercial process, helped to spur the development of the principles of physical chemistry that account for the effects of temperature and pressure on chemical equilibrium and kinetics. The ammonia synthesis reaction is strongly equilibrium limited. The equilibrium conversion to ammonia is favored by high pressure and low temperature. Haber therefore recognized that the key to a successful process for making ammonia from hydrogen and nitrogen was a catalyst with a high activity to allow operation at low temperatures where the equilibrium is relatively favorable.

Bosch and co-workers devised laboratory reactors to operate at high pressure and temperature in a recycle mode. These test reactors had the essential characteristics of potential industrial reactors and were used by Mittasch and co-workers to screen some 20,000 samples as candidate catalysts. The results led to the identification of an iron-containing mineral that is similar to today's industrial catalysts. The researchers recognized the need for porous catalytic materials and materials with more than one component, today identified as the support, the catalytically active component, and the promoter. Today's technology for catalyst testing has become more efficient because much of the test equipment is automated, and the analysis of products and catalysts is much faster and more accurate.

Homogeneous Catalysis

CHARACTERIZATION OF SOLUTION PROCESSES

There are many important examples of catalysis in the liquid phase, but catalysis in the gas phase is unusual. From an engineering viewpoint, most of the liquid-phase processes have the following characteristics in common.

Pressure and Temperature. The pressure and temperature are relatively low, typically less than about 2 MPa (20 atm) and 150°C. High pressures are used in some applications, but they require expensive thick-walled reactors. High temperatures are largely avoided because they result in high autogenous pressures and because many of the catalysts are unstable at high temperatures.

Corrosiveness. The catalyst solutions are corrosive, and the reactors, separation devices, etc that come in contact with them must be made of expensive corrosion-resistant materials.

Separation Processes. Separation of the catalyst from the products is a significant expense; the process flow diagram and the processing cost are often dominated by the separations. Many soluble catalysts are expensive, eg, rhodium complexes, and must be recovered and recycled with high efficiency. The most common separation devices are distillation columns; extraction is also applied.

Gas Handling. The reactants are often gaseous under ambient conditions. To maximize the rate of the catalytic reaction, it is often necessary to minimize the resistance to gas–liquid mass transfer, and the gases are therefore introduced as swarms of bubbles into a well-stirred liquid or into devices such as packed columns that facilitate gas–liquid mixing and gas absorption.

Exothermicity. The catalytic reactions are often exothermic bond-forming reactions of small molecules that give larger molecules. Consequently, the reactors are designed for efficient heat removal. They may be jacketed or contain coils for heat-transfer media, or the heat of reaction may be used to vaporize the products and aid in the downstream separation by distillation.

There are also a number of generalizations about the chemistry of these processes. Often the reactants are small building blocks, many formed from organic raw materials, namely, petroleum, natural gas, and coal. The reactants include O₂, low molecular-weight olefins, and synthesis gas (CO and H₂). In older technology, acetylene was a common building block. Many reactions are catalyzed by acids and bases, usually in aqueous solution. Many reactions are catalyzed by organometallic compounds, usually in nonaqueous organic solvents. The organometallic catalysts used in technology are often highly selective.

INFLUENCE OF MASS TRANSPORT ON REACTION RATES

When a relatively slow catalytic reaction takes place in a stirred solution, the reactants are supplied to the catalyst from the immediately neighboring solution so readily that virtually no concentration gradients exist. The intrinsic chemical kinetics determines the rate of the reaction. However, when the intrinsic rate of the reaction is very high and or the transport of the reactant slow, as in a viscous polymer solution, the concentration gradients become significant, and the transport of reactants to the catalyst cannot keep the catalyst supplied sufficiently for the rate of the reaction to be that corresponding to the intrinsic chemical kinetics. Assume that the transport of the reactant in solution is described by Fick's law of diffusion with a diffusion coefficient *D*, and the intrinsic chemical kinetics is of the following form

$$r = k[C][A]$$
(1)

where *C* is catalyst and *A* the reactant. Then in the general case in which the diffusion influences the rate (8),

$$\eta = \frac{r}{r_{\max}} = \frac{1}{1 + \frac{k}{4\pi \left(\frac{R_A + R_B}{2}\right) D}}$$
(2)

where η, the ratio of the reaction rate to the maximum value that could occur, ie, the rate in the absence of a transport influence, is called the effectiveness

factor, and R_C and R_A are the radii of the catalyst and reactant molecules, respectively. There are two limiting cases; if $k \ll 4\pi(\frac{R_A+R_B}{2})D$, then there is no diffusion influence and the rate is described by equation 1, where the concentrations are the bulk average concentrations in the solution. On the other hand, when the inequality is inverted, the rate becomes

$$r = 4\pi\left(\frac{R_A + R_B}{2}\right) D[C][A] \tag{3}$$

In the former case, the rate is independent of the diffusion coefficient and is determined by the intrinsic chemical kinetics; in the latter case, the rate is independent of the rate constant k and depends on the diffusion coefficient; the reaction is then diffusion controlled. This is a different kind of mass transport influence than that characteristic of a reactant from a gas to a liquid phase.

EXAMPLES OF SOLUTION CATALYSIS

Acid–Base Catalysis. Inexpensive mineral acids, eg, H_2SO_4 , and bases, eg, KOH, in aqueous solution are widely applied as catalysts in industrial organic synthesis. Catalytic reactions include esterifications, hydrations, dehydrations, and condensations. Much of the technology is old and well established, and the chemistry is well understood. Reactions that are catalyzed by acids are also typically catalyzed by bases. In some instances, the kinetics of the reaction has a form such as the following (9):

$$r = \left(k_o[H_2O] + k_H[H^+] + k_{HA}[HA] + k_{OH}[OH^-] + k_B[B] \right) [R] \tag{4}$$

where r is the reaction rate, $[R]$ the concentration of the reactant, and the terms on the right-hand side represent catalysis by water, hydrogen ions, undissociated acid HA, etc. Often all the terms but one are negligible.

If the second term in equation 4 is the only significant one, then catalysis is by hydrogen ions (hydrated protons), and the catalysis is called specific acid catalysis; the rate of the reaction is proportional to the concentration of the hydrogen ions and to the concentration of the reactant. Many examples conform to this pattern. Similarly, if the third term on the right-hand side of equation 4 is the only significant one, then the catalysis is by HA, and general acid catalysis occurs. If the fourth term is the significant one, hydroxide ions are the catalyst and specific base catalysis occurs. If the fifth term is the significant one, general base catalysis occurs.

The chemistry of acid–base catalysis involves the transfer of hydrogen ions, H^+ and sometimes H^- . In general or specific acid catalysis, the undissociated acid molecules or the hydrated protons formed by dissociation of an acid, respectively, donate protons to the reactant. The proton acceptor in an aqueous solution is a good base, often an organic compound including O, N, or S. In catalysis by bases, the reactant donates a proton to the catalyst. The proton donor in general acid catalysis may be a weak or a strong acid, and often the activity of the catalyst increases with its strength as an acid, measured by the acid dissociation constant K_a .

Donation of a proton to the reactant often forms a carbenium ion or an oxonium ion, which then reacts in the catalytic cycle. For example, a catalytic cycle suggested for the conversion of phenol and acetone into bisphenol A, which is an important monomer used to manufacture epoxy resins and polycarbonates, in an aqueous mineral acid solution is shown in Figure 1 (10).

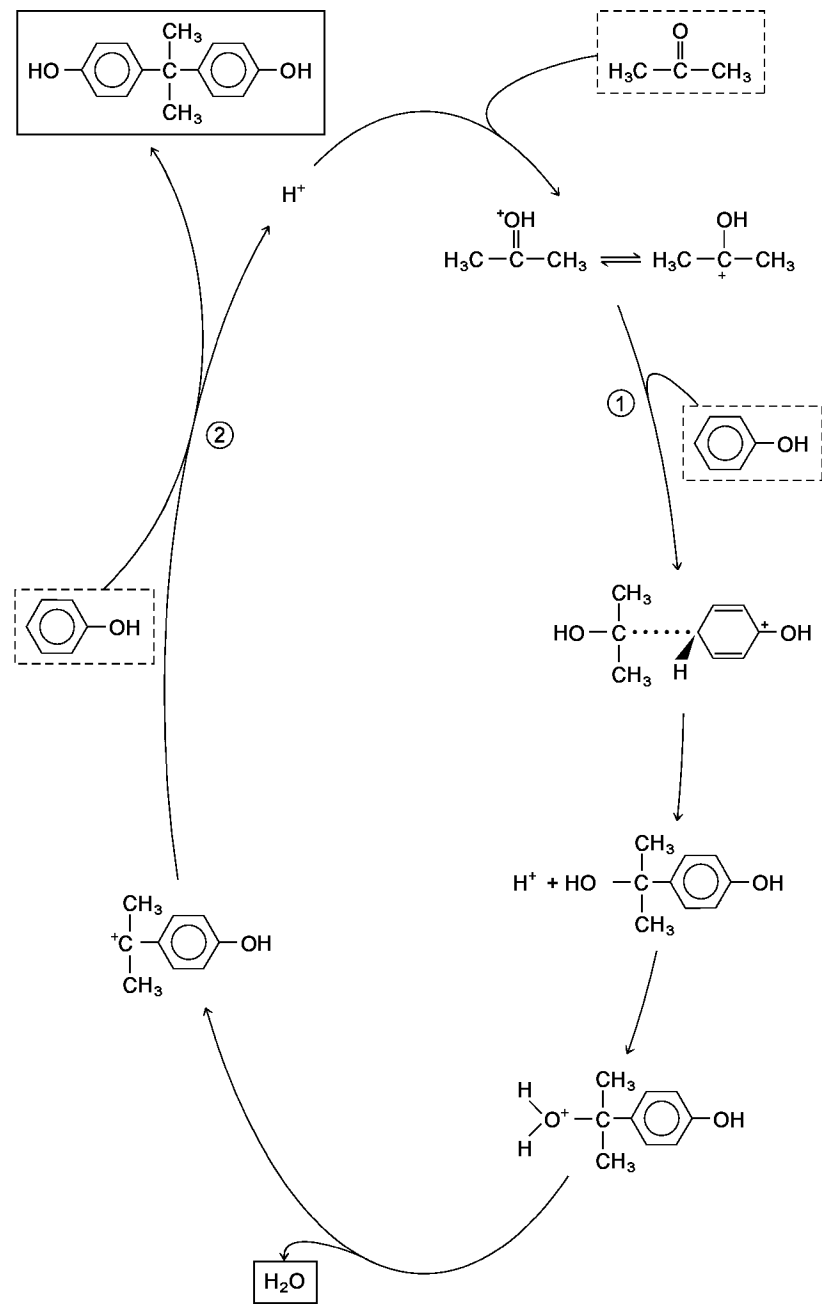


Fig. 1. Catalytic cycle for synthesis of bisphenol A from phenol and acetone in the presence of a dissociated mineral acid (10).

The kinetics of the bisphenol A synthesis has been reported to be of the following form (11)

$$r = k[H^+][A][P] \tag{5}$$

where *A* is acetone and *P* is phenol. When the reaction is carried out in the presence of low concentrations of an added compound, thioglycolic acid, HSCH₂COOH, the rate is increased with the kinetics reported to be of the following form (12)

$$r = k'[H^+][A][P](k_1 + k_2[T]) \tag{6}$$

where *T* is thioglycolic acid, a promoter. A catalyst promoter is a substance that, although it lacks significant catalytic activity itself, increases the activity, or possibly the selectivity, of a catalyst. Promoters are common in catalysis.

In some processes the reactant bases are too weak to be protonated significantly except in the presence of very strong acids such as fuming sulfuric acid or a mixture of concentrated sulfuric and nitric acids, ie, mixed acid. Nitration of toluene, for example, requires such solutions; two liquid phases are present in the reactor.

The kinetics of reactions catalyzed by very strong acids are often complicated. The exact nature of the proton donor species is often not known, and typically the rate of the catalytic reaction does not have a simple dependence on the total concentration of the acid. However, sometimes there is a simple dependence of the catalytic reaction rate on some empirical measure of the acid strength of the solution, such as the Hammett acidity function *H*₀, which is a measure of the tendency of the solution to donate a proton to a neutral base. Sometimes the rate is proportional to *b*₀ (−log*b*₀). Such a dependence may be expected when the slow step in the catalytic cycle is the donation of a proton by the solution to a neutral reactant, ie, base; but it is not easy to predict when such a dependence may be found.

An important petroleum refining process, alkylation of propylene or butenes with isobutane to give high octane-number branched products, is catalyzed by concentrated sulfuric acid or hydrofluoric acid. The reactions are carried out at subambient temperatures, at which the equilibrium is favorable, in stirred, refrigerated reactors containing two-phase liquid mixtures. Most of the hydrocarbon reactants are in the organic phase, and, when the catalyst is H₂SO₄, most of the catalyst is in the aqueous phase; the reaction takes place near the liquid–liquid interface (see *ALKYLATION*).

In the alkylation process, the reactants are weak bases. The stronger bases in the mixture, the olefins, are protonated, forming carbenium ions. The carbenium ions are good Lewis acids, and they react with isobutane, a good hydride ion donor, to form paraffins and the relatively stable *t*-butyl cation, ie, trimethyl carbenium ion. This is a hydride transfer reaction; such reactions are important in many acid catalyzed hydrocarbon conversions. The *t*-butyl cation becomes the predominant carbenium ion in the organic solution and reacts with propylene or butenes in Lewis acid–Lewis base reactions to form carbon–carbon bonds, giving C₇ or C₈ products among others. There are many C₇ and C₈ isomers formed because isomerizations are rapid. A partial cycle

that illustrates the important characteristics of alkylation is shown in Figure 2 for the ethylene–isobutane alkylation. The cycle is shown for ethylene because it gives a simpler product distribution than propylene or butenes; ethylene is much less reactive than propylene or butenes because on protonation it forms a primary carbenium ion, which is much less stable than the secondary carbenium ion formed by protonation of propylene or straight-chain butenes. Ethylene is not used in the commercial alkylation processes.

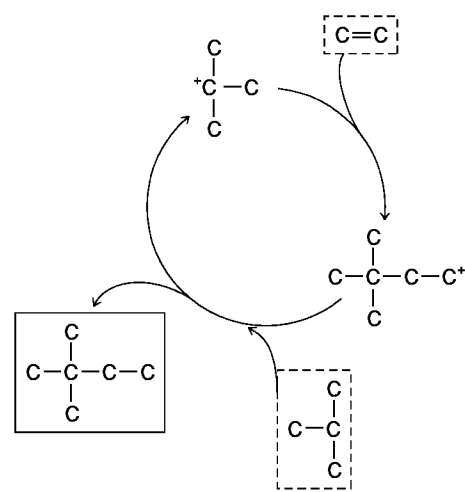


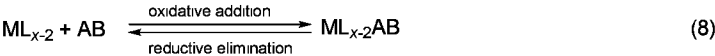
Fig. 2. Catalytic cycle for the ethylene–isobutane alkylation (10).

Acid catalyzed reactions of paraffins require much stronger acids than those of olefins and aromatics, because the paraffins are much weaker bases. The only acids that catalyze reactions of paraffins alone at relatively low temperatures are called superacids (13), combinations of Brønsted and Lewis acids; examples include $\text{HCl} + \text{AlCl}_3$, $\text{HF} + \text{SbF}_5$, and $\text{FSO}_3\text{H} + \text{SbF}_5$ (magic acid). Superacids are much stronger acids than concentrated sulfuric acid and some have values of H_0 of -20 and less, whereas that of concentrated sulfuric acid is about -12 . The Hammett acidity function is logarithmic; thus some superacids are more than eight orders of magnitude stronger proton donors than sulfuric acid. Hence the superacids can protonate paraffins, even methane. They catalyze isomerization and carbon–carbon bond-forming and bond-breaking reactions at low temperatures but are not found in commercial applications, in part because of their extreme corrosiveness. Solid catalysts with superacidic character are much more important in practice.

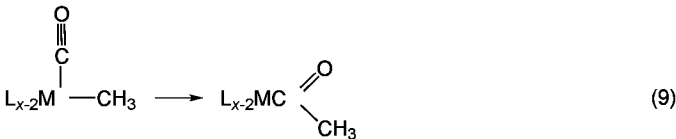
Organometallic Catalysis. Most of the recent innovations in industrial homogeneous catalysis have resulted from discoveries of organometallic catalysts. Thousands of organometallic compounds (complexes), ie, those with metal–carbon bonds, are known, and the rapid development of organotransition metal chemistry in recent years has been motivated largely by the successes and opportunities in catalysis. The chemistry of organotransition metal catalysis is explained by the bonding and reactivity of organic groups (ligands) bonded to the metals. The d orbitals of the metals allow bonding of ligands such as H (hydride), CO , and olefins in ways that facilitate their reaction. The important reactions in catalytic cycles are those of ligands bonded in the coordination sphere of the same metal atom. Bonding of ligands such as CO or olefin to a transition metal activates them and facilitates the catalysis. The following reactions of transition-metal complexes account for almost all the steps in the catalytic cycles.



where M is metal and L and L' are ligands. This reaction may be thermally or photochemically initiated; it usually proceeds by dissociation of a ligand to give a coordinatively unsaturated complex, to which another ligand is then bonded. This is a ligand dissociation–association sequence, and it is one way in which reactants are bonded to catalysts.



This reaction requires a metal complex that is coordinatively unsaturated and provides another way for bonding of reactant ligands to a metal.



In this reaction one ligand is inserted between the metal and another ligand, creating a site of coordinative unsaturation so that another reactant ligand can be associated with the metal. The insertion reaction accounts for the chain-growth steps of olefin polymerization reactions.

Wilkinson Hydrogenation. One of the best understood catalytic cycles is that for olefin hydrogenation in the presence of phosphine complexes of rhodium, the Wilkinson hydrogenation (14,15). The reactions of a number of olefins, eg, cyclohexene and styrene, are rapid, taking place even at room temperature and atmospheric pressure; but the reaction of ethylene is extremely slow. Complexes of a number of transition metals in addition to rhodium are active for the reaction.

The Wilkinson hydrogenation cycle shown in Figure 3 (16) was worked out in experiments that included isolation and identification of individual rhodium complexes, measurements of equilibria of individual steps, determination of rates of individual steps under conditions of stoichiometric reaction with certain reactants missing so that the catalytic cycle could not occur, and determination of rates of the overall catalytic reaction. The cycle demonstrates some generally important points about catalysis: the predominant species present in the reacting solution and the only ones that are easily observable by spectroscopic methods, eg, $\text{RhCl}[\text{P}(\text{C}_6\text{H}_5)_3]_3$, $\text{RhCl}[\text{P}(\text{C}_6\text{H}_5)_3]_2$ (olefin), and $\text{RhCl}_2[\text{P}(\text{C}_6\text{H}_5)_3]_4$, are outside the cycle, possibly in virtual equilibrium with species in the cycle, and not involved in the kinetically significant steps of the cycle. Often the only species that can be observed during catalysis are those that are not involved in the cycle. Consequently, elucidation of catalytic cycles is difficult, and inferences about cycles that are based on easily measured compositions of reacting solutions are usually less than well founded. The exceptions to this rule are usually the cycles of least interest, those of slow catalytic reactions.

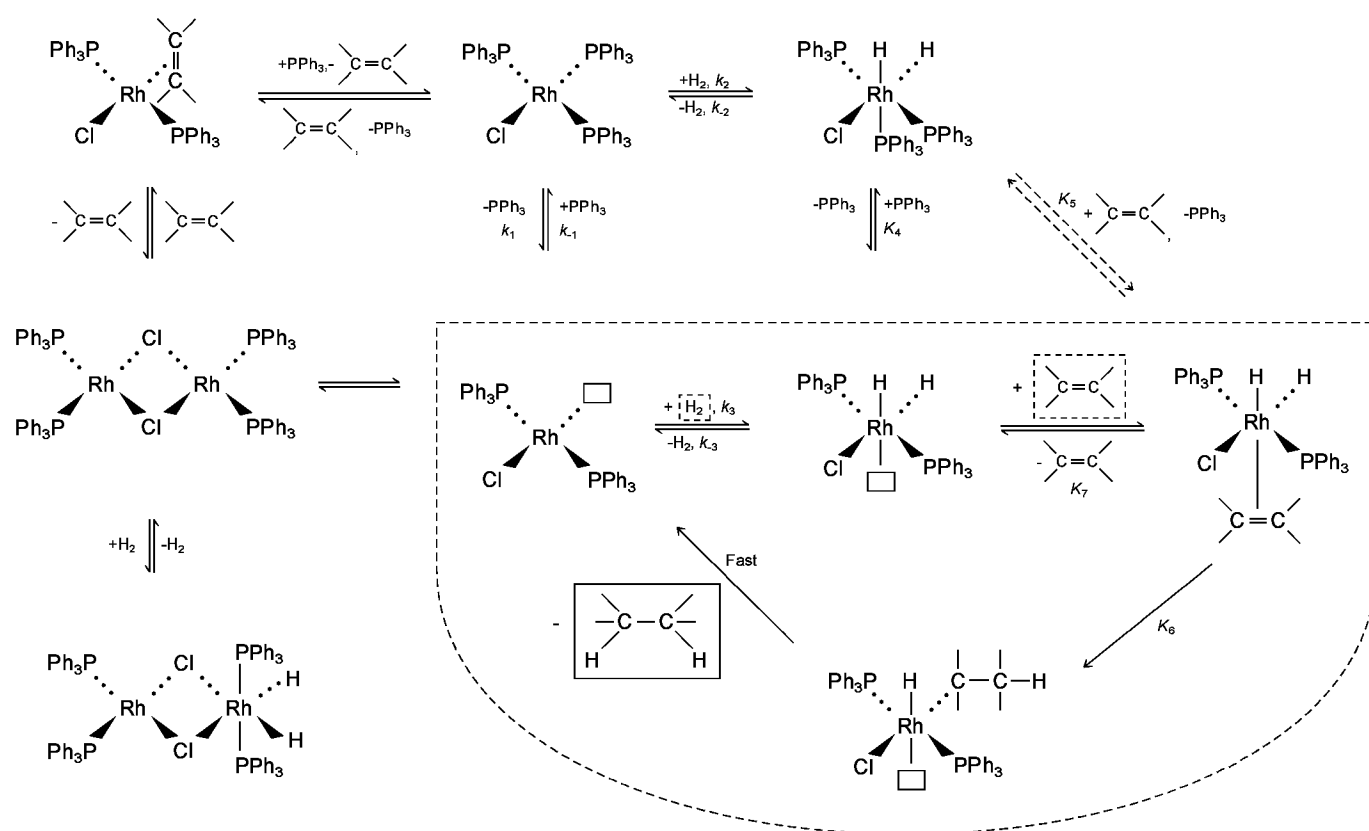
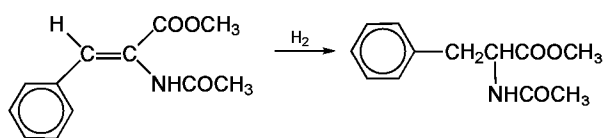


Fig. 3. Catalytic cycle (within dashed lines) for the Wilkinson hydrogenation of olefin (14,16). Ph represents phenyl (C_6H_5). Values of rate constants and equilibrium constants are as follows: $k_1 = 0.68 \text{ s}^{-1}$; $k_{-1} > 7 \times 10^4 \text{ L (mol}\cdot\text{s)}$; $K_1 < 10 \text{ mol L}^{-1}$; $k_2 \sim 1$; $k_{-2} = 3 \times 10^{-4}$; $k_3 = 4.8 \text{ L (mol}\cdot\text{s)}$; $k_4 = 2.8 \times 10^{-4} \text{ s}^{-1}$; $K_2 = 1.7 \times 10^4 \text{ L (mol}\cdot\text{s)}$; $k_5 > 7 \times 10^4 \text{ L (mol}\cdot\text{s)}$; $k_6 = 0.22 \text{ s}^{-1}$.

The Wilkinson hydrogenation illustrates the roles of the oxidative addition, reductive elimination, and insertion reactions, all of which occur in the cycle (Fig. 3). Some of the properties of the rhodium phosphine complexes that explain their success as catalysts include the following: Rhodium exists in two stable oxidation states, Rh(I) and Rh(III), separated by two units. Oxidative addition and reductive elimination reactions require changes of two units in metal oxidation state. There are no intermediates that are so stable that they form bottlenecks in the cycle. There is an exquisite dynamic balance, and the cycle turns over rapidly with only low concentrations of the intermediates being present in a steady state. The phosphines are electron donor ligands that are important in controlling the reactivities of the intermediates and regulating the dynamic balance. Replacement of triphenylphosphine by other phosphines leads to significant changes in the rate of the catalytic hydrogenation. The phosphines can influence the reactivities of the intermediates, and thus the rate of catalysis, by virtue of both electronic and steric effects.

Chiral Hydrogenation. Biological reactions are stereoselective, and numerous drugs must be pure optical isomers. Metal complex catalysts have been found that give very high yields of chiral products, and some have industrial application (17,18). The hydrogenation of the methyl ester of acetamidocinnamic acid has been carried out to give a precursor of L-dopa, ie, 3,4-dihydroxyphenylalanine, a drug used in the treatment of Parkinson's disease.



The strategy of the catalyst development was to use a rhodium complex similar to those of the Wilkinson hydrogenation but containing bulky chiral ligands in an attempt to direct the stereochemistry of the catalytic reaction to favor the desired L isomer of the product (17). Active and stereoselective catalysts have been found and used in commercial practice, although there is now a more economical route to L-dopa than through hydrogenation of the prochiral precursor.

Two pathways were found for the chiral hydrogenation, and they give products with different stereochemistries (19). One pathway involves the preferred mode of initial binding of the reactant to the catalyst. The other pathway involves an isomer of the reactant-catalyst complex that is formed in only small amounts, but its conversion is energetically favorable and constitutes the kinetically predominant pathway to products (9) (Fig. 4). Thus the chirality of the product is determined not by the preferred mode of the initial binding, but instead by the more favorable energetics of the pathway involving the minor isomer of the reactant-catalyst complex.

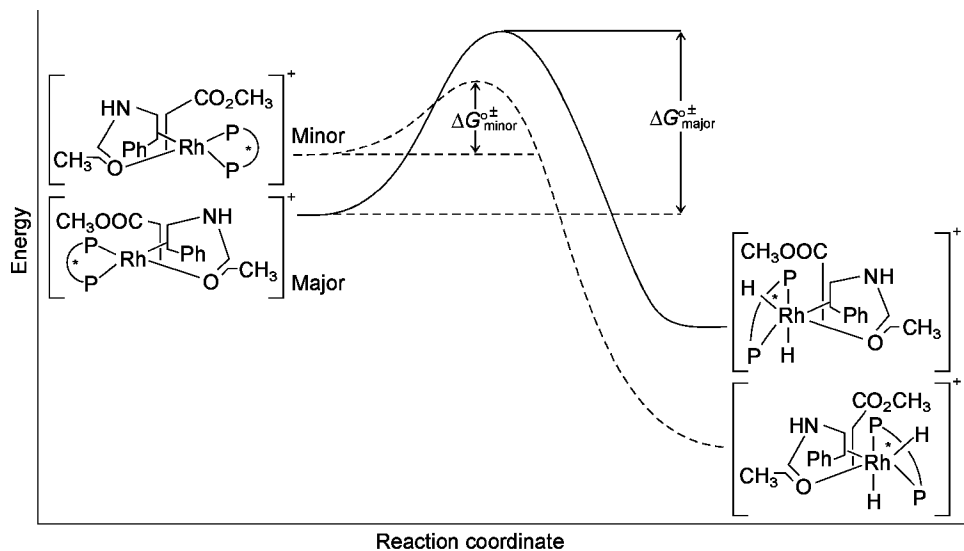


Fig. 4. Schematic representation of energy profiles for the pathways for the hydrogenation of a prochiral precursor to make L-dopa (19). The chiral disphosphine ligand is shown schematically as P^*P . Ph represents phenyl.

Methanol Carbonylation. An important industrial process catalyzed by rhodium complexes in solution is methanol carbonylation to give acetic acid.



The catalytic cycle (Fig. 5) (20) is well established, although the details of the conversion of the intermediate CH_3COI and methanol into the product are not well understood; the mechanism is not shown for this part of the cycle, but it probably involves rhodium in a catalytic role. The CH_3I works as a cocatalyst or promoter because it undergoes an oxidative addition with $[\text{Rh}(\text{CO})_2\text{I}_2]$, and the resulting product has the CO ligand bonded cis to the CH_3 ligand; these two ligands are then poised for an insertion reaction.

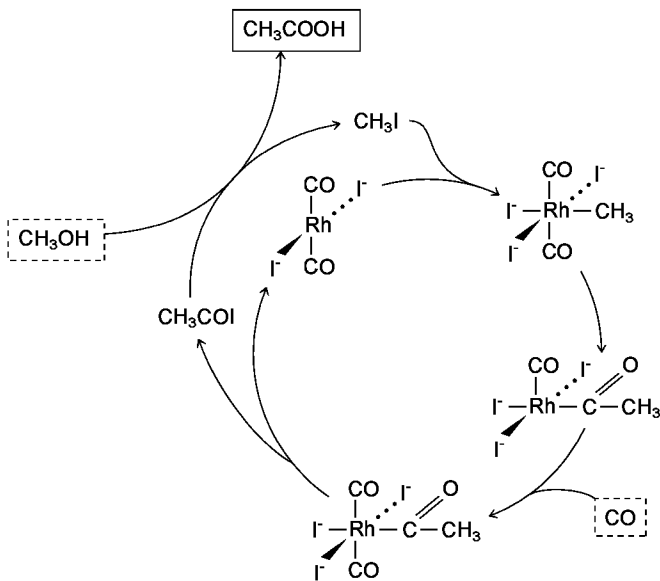


Fig. 5. Catalytic cycle for methanol carbonylation (20).

Methanol carbonylation is one of only a few industrially important catalytic reactions for which the quantitative reaction kinetics is known (21).

$$r = k[\text{CH}_3\text{I}][\text{Rh complex}] \tag{11}$$

where $k = 3.5 \times 10^6 \exp(-E_{act}/RT)$ and R is the gas constant, T is the absolute temperature, and E_{act} is 61.5 kJ/mol (14.7 kcal/mol). Because the reaction is zero-order in the reactants, a stirred reactor has no disadvantage in comparison with a tubular flow reactor with respect to the efficient use of the reactor volume. A stirred reactor might therefore be preferred to facilitate rapid heat transfer and good gas-liquid contacting for rapid gas-liquid mass transfer, ie, dissolution of the CO into the reactant solution.

The reaction is carried out in a polar solvent, as the intermediates are anionic. Water is present from the following reaction, which achieves virtual equilibrium:



Water is also formed in the acid catalyzed dehydration of methanol to give dimethyl ether. The solution is acidic because of the presence of the HI. The process flow diagram (22) (Fig. 6) is characteristic of those for homogeneous catalytic processes in being dominated by the separations devices. The products are purified by distillation, and several columns are required because the boiling point of the product acetic acid is near the middle of the boiling range of the product mixture; both the light products, including unconverted CO, CH_3I , and dimethyl ether, and the heavy rhodium complex must be recovered and recycled efficiently for the process to be economical. Corrosion is also a concern, and the reactor, separations devices, and lines are made of expensive stainless steel alloys.

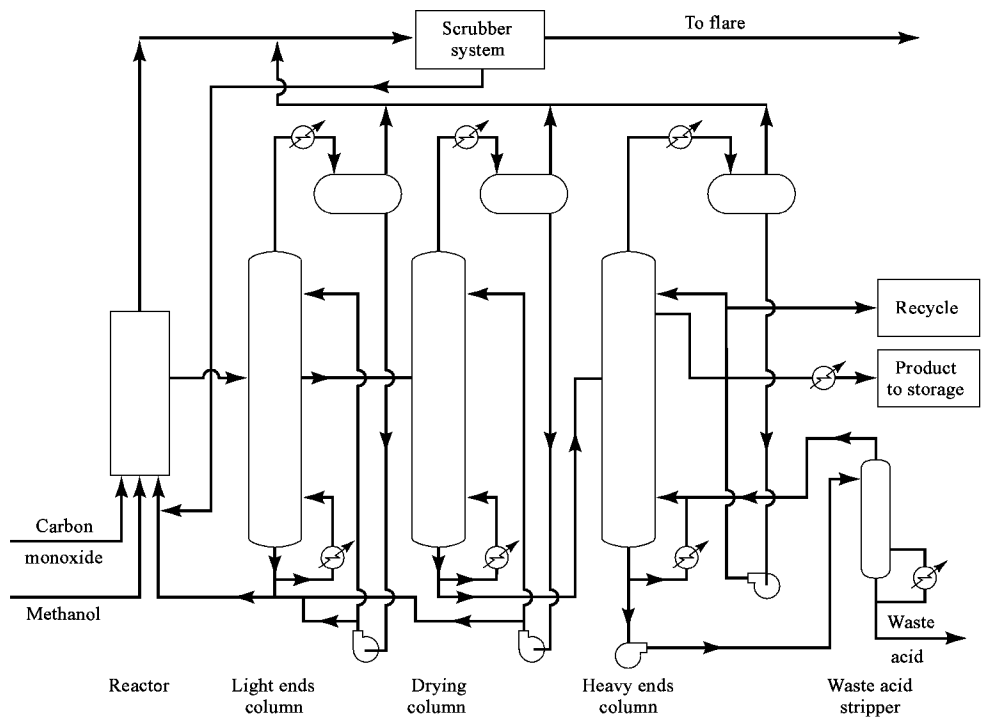
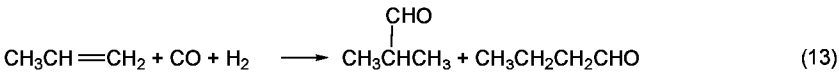


Fig. 6. Process flow diagram for methanol carbonylation to make acetic acid (22).

Olefin Hydroformylation (The Oxo Process). One of the most important industrial applications of transition-metal complex catalysis is the hydroformylation of olefins (23), illustrated for propylene:

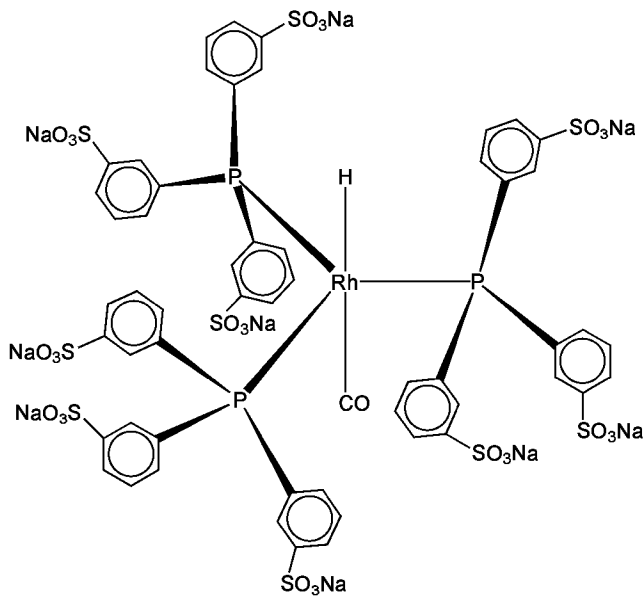


The linear isomer is more valuable than the branched isomer (see BUTYRALDEHYDE). The product aldehydes are hydrogenated to give so-called oxo alcohols; long-chain products are converted into sulfonates and used as detergents.

The oxo process was discovered in 1938 by Roelen and co-workers of Ruhr chemie. The first catalysts were cobalt carbonyl complexes formed from $[\text{HCo}(\text{CO})_4]$. They are still used on a large scale. The process is carried out at temperatures of 150°C and pressures of >30 MPa (several hundred atm). The high pressures are required to maintain the cobalt in the form of the soluble metal carbonyl complex; at lower pressures, cobalt metal can form and deposit on the reactor walls, possibly in a porous form that adds a significant resistance to heat transfer. Use of cobalt complexes with phosphine ligands led to processes with improved selectivities. The process flow diagram is complicated because it is expensive to separate the catalyst from the products and recycle it in the high pressure process. In the Kuhlmann process (10,24), the catalyst is extracted into an aqueous stream and then regenerated with acid to give $[\text{HCo}(\text{CO})_4]$, which is absorbed into the reactant solution.

A significant advance in hydroformylation technology was made with the discovery that phosphine complexes of rhodium, similar to those used in the Wilkinson hydrogenation but incorporating H, CO, and olefin ligands as well as triphenylphosphine, have catalytic activities several orders of magnitude greater than those of cobalt; furthermore, the rhodium complexes are stable enough to be used at low pressures, typically 1.5 MPa (15 atm) at about 150°C, and separated by distillation (25,26). Rhodium complex catalysts now are used in industrial processes for hydroformylation of propylene. When a large excess of triphenylphosphine is used as the solvent, the selectivity for the desired straight-chain product is high, with >95% of the aldehyde being *n*-butyraldehyde.

The processing costs associated with separation and corrosion are still significant in the low pressure process; for the process to be economical, the efficiency of recovery and recycle of the rhodium must be very high. Consequently, researchers have continued to seek new ways to facilitate the separation and confine the corrosion. Extensive research was done with rhodium phosphine complexes bonded to solid supports, but the resulting catalysts were not sufficiently stable, as rhodium was leached into the product solution (27,28). A more successful solution to the engineering problem resulted from the application of a two-phase liquid-liquid process (29). The catalyst is synthesized with polar $-\text{SO}_3\text{Na}$ groups on the phenyl rings of the triphenylphosphine.



so that it is water soluble. In the reactor, the catalyst is largely confined to the aqueous phase and the reactants are largely confined to the organic phase;

reaction likely takes place near the interface. A process flow diagram is shown in Figure 7 (29). The two liquid phases are separated downstream of the stirred reactor and the catalyst is recycled with a high efficiency. The process is applied commercially and seems to be competitive with the single-phase process.

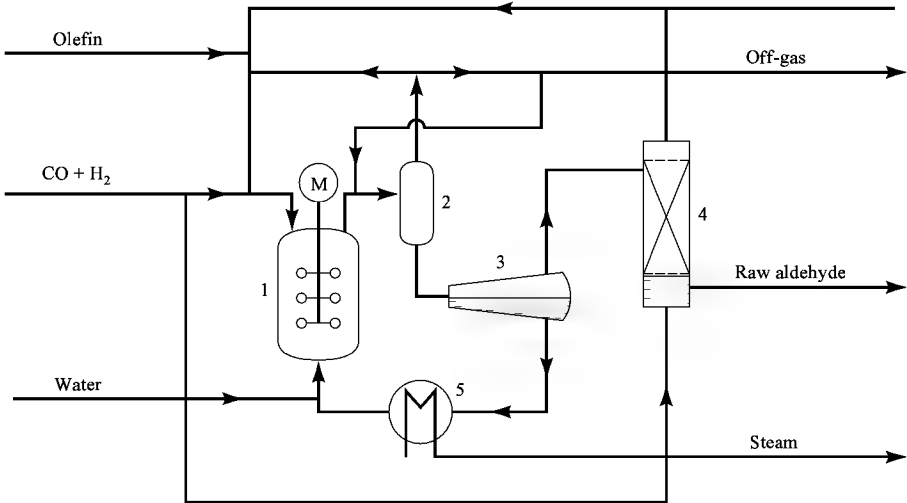
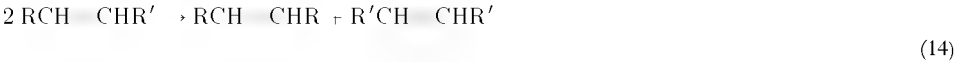


Fig. 7. Process flow diagram for the two-phase hydroformylation of propylene where 1 = reactor; 2 = separator; 3 = phase separator; 4 = stripping column; and 5 = heat exchanger (29).

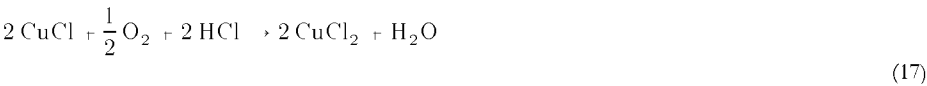
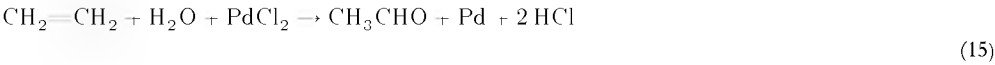
Olefin Metathesis. The olefin metathesis (dismutation) reaction (30), discovered by Eleuterio (31), converts olefins to lower and higher molecular weight olefins. For example, propylene is converted into ethylene and butene



This reaction is catalyzed in solution by complexes of tungsten, molybdenum, or rhenium in high oxidation states, eg, Re^{7+} . Examples of active catalysts are $[\text{W}(\text{CH-}i\text{-C}_4\text{H}_9)(\text{OR})_2\text{X}_2]$, where X is halide (32), and $[\text{W}(\text{CH-}i\text{-C}_4\text{H}_9)(\text{NAr})(\text{OR})_2]$, where Ar is aromatic (33). A number of catalysts require cocatalysts such as $\text{CH}_3\text{Al}_2\text{Cl}_3$.

The olefins that undergo metathesis include most simple and substituted olefins; cyclic olefins give linear high molecular-weight polymers. The mechanism of the reaction is believed to involve formation of carbene complexes that react via cyclic intermediates, ie, metallacycles. Industrial olefin metathesis processes are carried out with solid catalysts (30).

The Wacker Oxidation of Ethylene to Acetaldehyde. One of the early industrial examples of organometallic catalysis in solution was described by Smidt and co-workers in 1959. This is the Wacker oxidation of ethylene to give acetaldehyde (qv) (26). It had long been known that Pd(II) complexes in solution would stoichiometrically oxidize ethylene to acetaldehyde. Smidt's insight was to make this reaction part of a catalytic cycle. The researchers created a process by closing the cycle, using an excess of an oxidizing agent, Cu^{2+} , to rapidly reoxidize the palladium that oxidized the ethylene and thereby keep palladium from plating out on the reactor walls as metal. The cycle is completed as O_2 reoxidizes the Cu^+ formed from Cu^{2+} . The sequence of reactions is the following:



These reactions constitute the cycle; their sum gives the stoichiometry of the Wacker oxidation:



This process is unusual among those involving organometallic chemistry in that it takes place in aqueous solution. In one process design there is a single reactor in which all three reactions in the sequence take place, and the feed contains pure O_2 . In another process, there are two reactors, with the ethylene oxidation, (eq. 15), and the palladium reoxidation, (eq. 16), taking place in one reactor and the reoxidation of Cu^+ with air taking place in the other. An advantage of the single-reactor process is the confinement of the corrosive solutions in one vessel, but this is compensated by the need for purified oxygen. The feed gas contains ethylene and oxygen, and the composition must be kept outside the explosive limits. Consequently, the feed gas is not a stoichiometric mixture, and gas recycle is necessary for economic operation. In contrast, the two-reactor process allows the use of air as a feed to the reactor where Cu^+ is reoxidized; the air flows once through the reactor and is almost all converted. Ethylene flows into the other reactor. A disadvantage of the two-reactor process is the need for corrosion-resistant materials in both reactors and the lines between them. Both designs have been successfully applied.

A process similar to the Wacker process has been applied for the oxidation of ethylene with acetic acid to give vinyl acetate, but now the principal applications are with a solid catalyst.

Free-Radical Oxidation of Hydrocarbons. The chemistry of the Wacker reaction is atypical for oxidation. A more common pattern in catalytic oxidation is a chain reaction proceeding through free-radical intermediates; hydroperoxides are common products, and they are often converted themselves into other products (34,35). Free-radical reactions are characterized by complex product distributions because O_2 has a high reactivity with organic reactants, with metal centers, and with many ancillary ligands. Metals typically play a role in an initiation process, helping to start a free-radical chain reaction; free radicals are often generated by metal-catalyzed decomposition of organic hydroperoxides. Some of the important applications of such chemistry are oxidations of petroleum-derived hydrocarbons. Catalysts include iron, manganese, cobalt, and copper in high oxidation states; a typical solvent is acetic acid. The processes include oxidation of *n*-butane to give acetic acid, formation of fatty acids from paraffin wax, and oxidation of cyclohexane to give adipic acid (qv) precursors in nylon manufacture.

A suggested mechanism of the cyclohexane oxidation is shown in Figure 8 (36). A free-radical chain is set up, with $\text{R}\cdot$ and $\text{ROO}\cdot$ being the chain carriers (R is C_6H_{11}), as shown in the upper right of the figure. One role of Co^{3+} is suggested to be that of an electron-transfer agent undergoing a

one-electron change; the role of the metal is that of a redox initiator, as cobalt cycles between the +2 and +3 oxidation states in a process that generates free radicals. As the cobalt also reacts in a cycle, its role is catalytic, and only small amounts are needed.

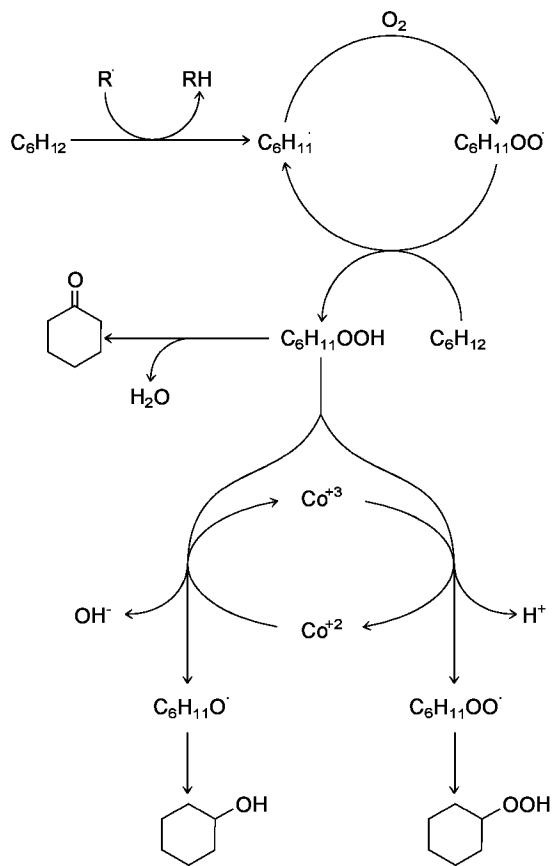
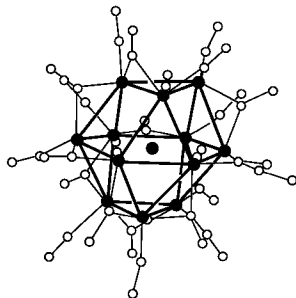


Fig. 8. Approximate mechanism for the free-radical oxidation of cyclohexane (36).

CO and H₂ Reactions. Synthesis gas (CO and H₂) can be converted into numerous organic chemicals, including acetic anhydride formed in a commercial process with a rhodium complex catalyst. Soluble rhodium catalysts are also active for synthesis of ethylene glycol along with methanol and other products (37,38). The process is not applied commercially because extremely high pressures are required. But the process is conceptually important because it is believed that the catalysts may be compounds with metal–metal bonds, called metal clusters. A simple metal cluster is [Rh₁₃(CO)₂₄H₃]²⁻, which has the following structure:



There are many related compounds, including rhodium carbonyl cluster anions, which are present in the solutions catalyzing ethylene glycol formation and which may be the catalytically active species or in equilibrium with them (38).

There are only a few well-documented examples of catalysis by metal clusters, and not many are to be expected as most metal clusters are fragile and fragment to give metal complexes or aggregate to give metal under reaction conditions (39). However, the metal carbonyl clusters are conceptually important because they form a bridge between catalysts commonly used in solution, ie, transition-metal complexes with single metal atoms, and catalysts commonly used on surfaces, ie, small metal particles or clusters.

PHASE-TRANSFER CATALYSIS

When two reactants in a catalytic process have such different solubility properties that they can hardly both be present in a single liquid phase, the reaction is confined to a liquid–liquid interface and is usually slow. However, the rate can be increased by orders of magnitude by application of a phase-transfer catalyst (40,41), and these are used on a large scale in industrial processing (see CATALYSTS, PHASE TRANSFER). Phase-transfer catalysts function by facilitating mass transport of reactants between the liquid phases. Often most of the reaction takes place close to the interface.

Industrial examples of phase-transfer catalysis are numerous and growing rapidly; they include polymerization, substitution, condensation, and oxidation reactions. The processing advantages, besides the acceleration of the reaction, include mild reaction conditions, relatively simple process flow diagrams, and flexibility in the choice of solvents.

Heterogeneous Catalysis

CHARACTERIZATION OF SURFACE PROCESSES

Most of the largest-scale catalytic processes take place with gaseous reactants in the presence of solid catalysts. From an engineering viewpoint, these processes offer the following advantages, in contrast to those involving liquid catalysts: (1) wide ranges of temperature and pressure are economically applied. The most direct way to increase the activity of a catalyst is to increase its temperature, and high temperatures can be used economically with solid catalysts as the reactants are gases and there is no liquid phase to require a high pressure. The catalysts must be robust to withstand the high temperatures;

solid catalysts are commonly used at temperatures of 500°C, and some endure temperatures several hundred degrees higher; (2) solid catalysts are only rarely corrosive; (3) the separation of gaseous or liquid products from solid catalysts is simple and costs little. It is simplest when the catalyst particles are confined in a fixed-bed reactor; when very small particles are used in a fluidized bed, they are entrained in the product stream, and a gas–solid separator is required; (4) the mixing and mass transport in a fixed- or fluidized-bed reactor are facilitated by the solid catalyst particles through which the reactants and products flow. If no liquid phase is present, a potentially significant mass-transfer resistance is eliminated; mass-transfer resistance in the gas phase is usually small. However, reactions take place on the internal surfaces of porous catalyst particles, and the resistance to transport through the pores is often significant; (5) strongly exothermic and strongly endothermic reactions are routinely carried out with solid catalysts. Fluidized-bed reactors offer the advantage of excellent mixing and high rates of heat transfer. They are commonly used when heat effects are large, for example, for oxidation reactions; alternatively, small tubes are used in bundles to minimize the distance through which the heat is transferred in a fixed bed. The catalyst particles themselves constitute a significant heat-transfer resistance, and the temperature gradients in particles are sometimes large.

PROPERTIES OF SOLID CATALYSTS

Most solid catalysts used on a large scale are porous inorganic materials. A number of these and the reactions they catalyze are summarized in Table 1 (10). Catalysis takes place as one or more of the reactants is chemisorbed, chemically adsorbed, on the surface and reacts there. The activity and selectivity of the catalyst depend strongly on the surface composition and structure.

Table 1. Some Large-Scale Industrial Processes Catalyzed by Surfaces of Inorganic Solids^a

Catalyst	Reaction
metals (eg, Ni, Pd, Pt, as powders or on supports) or metal oxides (eg, Cr ₂ O ₃)	C=C bond hydrogenation (eg, olefin + H ₂ → paraffin)
metals (eg, Cu, Ni, Pt)	C=O bond hydrogenation (eg, acetone + H ₂ → 2-propanol)
metal (eg, Pd, Pt)	complete oxidation of hydrocarbons, oxidation of CO
Fe, Ru (supported and promoted with alkali metals)	3 H ₂ + N ₂ → 2 NH ₃
Ni	CO + 3 H ₂ → CH ₄ + H ₂ O (methanation)
	CH ₄ + H ₂ O → 3 H ₂ + CO (steam reforming)
Fe or Co (supported and promoted with alkali metals)	CO + H ₂ → paraffins + olefins + H ₂ O + CO ₂ (+oxygen-containing organic compounds) (Fischer-Tropsch reaction)
Cu (supported on ZnO, with other components, eg, Al ₂ O ₃)	CO + 2 H ₂ → CH ₃ OH
Re + Pt (supported on ε-Al ₂ O ₃ and promoted with chloride)	paraffin dehydrogenation, isomerization and dehydrocyclization (eg, <i>n</i> -heptane→ toluene + 4 H ₂) (naphtha reforming)
solid acids (eg, SiO ₂ –Al ₂ O ₃ , zeolites)	paraffin cracking and isomerization; aromatic alkylation;
γ-Al ₂ O ₃	polymerization of olefins
Pd supported on zeolite	alcohol → olefin + H ₂ O
metal-oxide-supported complexes of Cr, Ti, or Zr	paraffin hydrocracking
metal-oxide-supported complexes of W or Re	olefin polymerization (eg, ethylene →polyethylene)
V ₂ O ₅ or Pt	olefin metathesis (eg, 2 propylene →ethylene + butene)
Ag (on inert support, promoted by alkali metals)	2 SO ₂ + O ₂ → 2 SO ₃
V ₂ O ₅ (on metal-oxide support)	ethylene + $\frac{1}{2}$ O ₂ → ethylene oxide (with CO ₂ + H ₂ O)
bismuth molybdate, uranium antimonate, other mixed metal oxides	naphthalene + $\frac{5}{2}$ O ₂ → phthalicanhydride + 2 CO ₂ + 2 H ₂ O
mixed oxides of Fe and Mo	<i>o</i> -xylene + 3 O ₂ → phthalic anhydride +3 H ₂ O
Fe ₃ O ₄ or metal sulfides	propylene + $\frac{1}{2}$ O ₂ → acrolein
$\left\{ \begin{array}{l} \text{Co-Mo } \gamma\text{-Al}_2\text{O}_3 \text{ (sulfided) } \\ \text{Ni-Mo } \gamma\text{-Al}_2\text{O}_3 \text{ (sulfided) } \\ \text{Ni-W } \gamma\text{-Al}_2\text{O}_3 \text{ (sulfided) } \end{array} \right\}$	propylene + $\frac{1}{2}$ O ₂ + NH ₃ →acrylonitrile + 3 H ₂ O
	CH ₃ OH + O ₂ → formaldehyde (with CO ₂ + H ₂ O)
	H ₂ O + CO → H ₂ + CO ₂ (water gas shift reaction)
	olefin hydrogenationaromatic
	hydrogenationhydrodesulfurizationhydrodenitrogenation

^a Ref. 10.

The catalysts with the simplest compositions are pure metals, and the metals that have the simplest and most uniform surface structures are single crystals. Researchers have done many experiments with metal single crystals in ultrahigh vacuum chambers so that unimpeded beams of particles and radiation can be used to probe them. These surface science experiments have led to fundamental understanding of the structures of simple adsorbed species, such as CO, H, and small hydrocarbons, and the mechanisms of their reactions (42); they indicate that catalytic activity is often sensitive to small changes in surface structure. For example, paraffin hydrogenolysis reactions take place rapidly on steps and kinks of platinum surfaces but only very slowly on flat planes; however, hydrogenation of olefins takes place at approximately the same rate on each kind of surface site.

A few industrial catalysts have simple compositions, but the typical catalyst is a complex composite made up of several components, illustrated schematically in Figure 9 by a catalyst for ethylene oxidation. Often it consists largely of a porous support or carrier, with the catalytically active components dispersed on the support surface. For example, petroleum refining catalysts used for reforming of naphtha have about 1 wt% Pt and Re on the surface of a transition alumina such as γ-Al₂O₃ that has a surface area of several hundred square meters per gram. The expensive metal is dispersed as minute particles or clusters so that a large fraction of the atoms are exposed at the surface and accessible to reactants (see CATALYSTS, SUPPORTED).

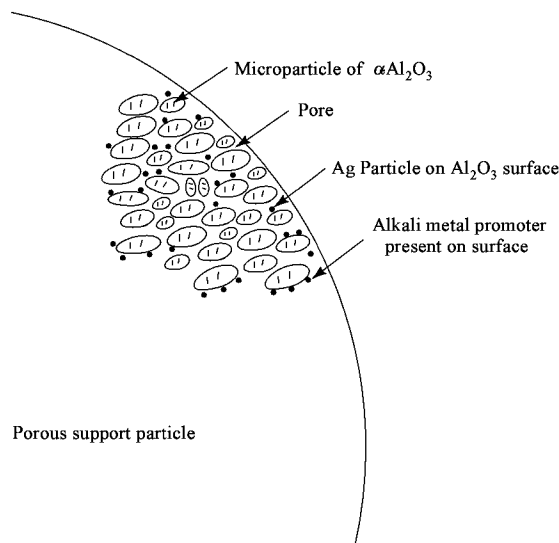


Fig. 9. Schematic representation of a catalyst for ethylene oxide synthesis (not to scale). The porous support particle consists of microparticles held together by a binder.

The typical industrial catalyst has both microscopic and macroscopic regions with different compositions and structures; the surfaces of industrial catalysts are much more complex than those of the single crystals of metal investigated in ultrahigh vacuum experiments. Because surfaces of industrial catalysts are very difficult to characterize precisely and catalytic properties are sensitive to small structural details, it is usually not possible to identify the specific combinations of atoms on a surface, called catalytic sites or active sites, that are responsible for catalysis. Experiments with catalyst poisons, substances that bond strongly with catalyst surfaces and deactivate them, have shown that the catalytic sites are usually a small fraction of the catalyst surface. Most models of catalytic sites rest on rather shaky foundations.

Important physical properties of catalysts include the particle size and shape, surface area, pore volume, pore size distribution, and strength to resist crushing and abrasion. Measurements of catalyst physical properties (43) are routine and often automated. Pores with diameters <2.0 nm are called micropores; those with diameters between 2.0 and 5.0 nm are called mesopores; and those with diameters >5.0 nm are called macropores. Pore volumes and pore size distributions are measured by mercury penetration and by N₂ adsorption. Mercury is forced into the pores under pressure; entry into a pore is opposed by surface tension. For example, a pressure of about 71 MPa (700 atm) is required to fill a pore with a diameter of 10 nm. The amount of uptake as a function of pressure determines the pore size distribution of the larger pores (44). In complementary experiments, the sizes of the smallest pores (those 1 to 20 nm in diameter) are determined by measurements characterizing desorption of N₂ from the catalyst. The basis for the measurement is the capillary condensation that occurs in small pores at pressures less than the vapor pressure of the adsorbed nitrogen. The smaller the diameter of the pore, the greater the lowering of the vapor pressure of the liquid in it.

Surface areas are determined routinely and exactly from measurements of the amount of physically adsorbed, physisorbed, nitrogen. Physical adsorption is a process akin to condensation; the adsorbed molecules interact weakly with the surface and multilayers form. The standard interpretation of nitrogen adsorption data is based on the BET model (45), which accounts for multilayer adsorption. From a measured adsorption isotherm and the known area of an adsorbed N₂ molecule, taken to be 0.162 nm², the surface area of the solid is calculated (see ADSORPTION).

INFLUENCE OF MASS TRANSPORT ON CATALYST PERFORMANCE

Reactants must diffuse through the network of pores of a catalyst particle to reach the internal area, and the products must diffuse back. The optimum porosity of a catalyst particle is determined by tradeoffs: making the pores smaller increases the surface area and thereby increases the activity of the catalyst, but this gain is offset by the increased resistance to transport in the smaller pores; increasing the pore volume to create larger pores for faster transport is compensated by a loss of physical strength. A simple quantitative development (46–48) follows for a first-order, isothermal, irreversible catalytic reaction in a spherical, porous catalyst particle.

If there is a significant resistance to transport of the reactant in the pores, a concentration gradient will exist at steady state, whereby the concentration of the reactant is a maximum at the particle periphery and a minimum at the particle center. The product concentration will be higher at the particle center than at the periphery. The concentration gradients provide the driving force for the transport.

As a reactant molecule from the fluid phase surrounding the particle enters the pore structure, it can either react on the surface or continue diffusing toward the center of the particle. A quantitative model of the process is developed by writing a differential equation for the conservation of mass of the reactant diffusing into the particle. At steady state, the rate of diffusion of the reactant into a shell of infinitesimal thickness minus the rate of diffusion out of the shell is equal to the rate of consumption of the reactant in the shell by chemical reaction. Solving the equation leads to a result that shows how the rate of the catalytic reaction is influenced by the interplay of the transport, which is characterized by the effective diffusion coefficient of the reactant in the pores, D_{eff} and the reaction, which is characterized by the first-order reaction rate constant.

The result is shown in Figure 10, which is a plot of the dimensionless effectiveness factor as a function of the dimensionless Thiele modulus ϕ , which is $R(\frac{k}{D_{eff}})^{1/2}$, where R is the radius of the catalyst particle and k is the reaction rate constant. The effectiveness factor is defined as the ratio of the rate of the reaction divided by the rate that would be observed in the absence of a mass transport influence. The effectiveness factor would be unity if the catalyst were nonporous. Therefore, the reaction rate is

$$r = \eta k [A]_s$$

(19)

where η is the effectiveness factor and $[A]$, the concentration of the reactant A at the peripheral surface of the catalyst particle. The observed reaction rate constant is not the intrinsic reaction rate constant k but the product ηk .

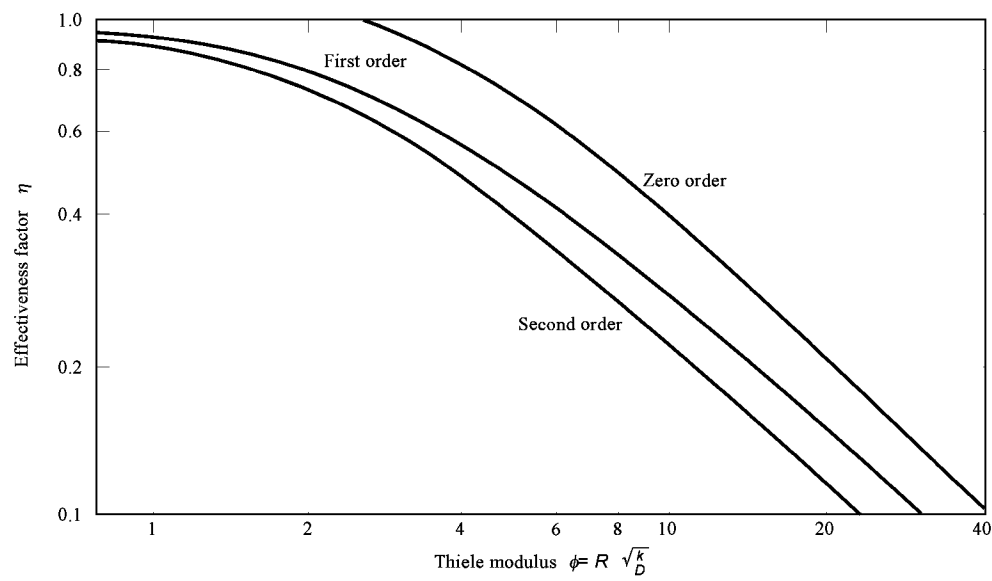


Fig. 10. The Thiele plot accounting for the influence of intraparticle mass transport on rates of catalytic reaction. The dimensionless terms η and ϕ are the effectiveness factor and the Thiele modulus, respectively, and are defined in the text.

Figure 10 shows that η is a unique function of the Thiele modulus. When the modulus ϕ is small ($\lesssim 1$), the effectiveness factor is unity, which means that there is no effect of mass transport on the rate of the catalytic reaction. When ϕ is greater than about 1, the effectiveness factor is less than unity and the reaction rate is influenced by mass transport in the pores. When the modulus is large ($\gtrsim 10$), the effectiveness factor is inversely proportional to the modulus, and the reaction rate (eq. 19) is proportional to $k \phi$, which, from the definition of ϕ , implies that the rate and the observed reaction rate constant are proportional to $(1/R)(D_{eff}k)^{1/2}[A]$. This result shows that both the rate constant, ie, a measure of the intrinsic activity of the catalyst, and the effective diffusion coefficient, ie, a measure of the resistance to transport of the reactant offered by the pore structure, influence the rate. It is not appropriate to say that the reaction is diffusion controlled; it depends on both the diffusion and the chemical kinetics. In contrast, as shown by equation 3, a reaction in solution can be diffusion controlled, depending on D but not on k .

In the case of a significant intraparticle diffusion influence, the temperature dependence of the observed rate constant, the apparent activation energy, is not that of the intrinsic rate constant, ie, the true activation energy; rather, as the Thiele modulus becomes large (> 10), the temperature dependence approaches that of $(D_{eff}k)^{1/2}$. The temperature dependence of a diffusion coefficient is usually small, and the measured activation energy is thus about half the intrinsic activation energy. This is an important and general result: the kinetics is disguised by the transport influence. When the effectiveness factor is unity, there is no disguise, and the true activation energy is measured.

This development has been generalized. Results for zero- and second-order irreversible reactions are shown in Figure 10. Results are given elsewhere (48) for more complex kinetics, nonisothermal reactions, and particle shapes other than spheres. For nonspherical particles, the equivalent spherical radius, three times the particle volume/surface area, can be used for R to a good approximation.

Even when there is a transport disguise, the reaction order remains one for a first-order reaction. But for reactions that are not intrinsically first order, the transport disguise changes the observed reaction order; for an intrinsically zero-order reaction, the observed order becomes $1/2$ and for an intrinsically second-order reaction it becomes $3/2$ when $\phi \gtrsim 10$. For all reaction orders the apparent activation energy is approximately half the intrinsic value in this limit.

The mass transport influence is easy to diagnose experimentally. One measures the rate at various values of the Thiele modulus; the modulus is easily changed by variation of R , the particle size. Crushing and sieving the particles provide catalyst samples for the experiments. If the rate is independent of the particle size, the effectiveness factor is unity for all of them. If the rate is inversely proportional to particle size, the effectiveness factor is less than unity and $\phi \gtrsim 10$. If the dependence is between these limits, then several experimental points allow triangulation on the curve of Figure 10 and estimation of η and ϕ . It is also possible to estimate the effective diffusion coefficient and thereby to estimate η and ϕ from a single measurement of the rate (48).

If the effectiveness factor is less than unity, the catalyst is not being used efficiently, ie, the central region is starved of reactant. The results of Figure 10 show how to increase the effectiveness factor: decrease the Thiele modulus. This can be done by some combination of the following: (1) decreasing the particle size R . However, if particles are too small, they may cause too great a pressure drop in a flow reactor or be entrained in the product stream; (2) changing particle shape to reduce the transport length. Particles with cross sections resembling clover leaves and wagon wheels have been used, for example; (3) increasing the effective diffusion coefficient. Larger catalyst pores accomplish this, but with a sacrifice in physical strength; and (4) decreasing the activity of the catalyst measured by k . This option is unappealing as researchers strive to make more active catalysts, but it may be economical to reduce the activity by reducing the loading of the catalytically active component on a support. It may also be appropriate to prepare the catalyst with the active component concentrated near the particle periphery and not in the particle interior.

Intraparticle mass transport resistance can lead to disguises in selectivity. If a series reaction $A \rightarrow B \rightarrow C$ takes place in a porous catalyst particle with a small effectiveness factor, the observed conversion to the intermediate B is less than what would be observed in the absence of a significant mass transport influence. This happens because as the resistance to transport of B in the pores increases, B is more likely to be converted to C rather than to be transported from the catalyst interior to the external surface. This result has important consequences in processes such as selective oxidations, in which the desired product is an intermediate and not the total oxidation product CO_2 .

Rates and selectivities of solid catalyzed reactions can also be influenced by mass transport resistance in the external fluid phase. Most reactions are not influenced by external-phase transport, but the rates of some very fast reactions, eg, ammonia oxidation, are determined solely by the resistance to this transport. As the resistance to mass transport within the catalyst pores is larger than that in the external fluid phase, the effectiveness factor of a porous catalyst is expected to be less than unity whenever the external-phase mass transport resistance is significant. A practical catalyst that is used under such circumstances is the ammonia oxidation catalyst. It is a nonporous metal and consists of layers of wire woven into a mesh.

CATALYST COMPONENTS

Industrial catalysts are typically complex in composition and structure. Catalytically active phases, supports, binders, and promoters comprise the components of the catalyst.

Catalytically Active Species. The most common catalytically active materials are metals, metal oxides, and metal sulfides. Occasionally, these are used in pure form; examples are Raney nickel, used for fat hydrogenation, and $\gamma\text{-Al}_2\text{O}_3$, used for ethanol dehydration. More often the catalytically active component is highly dispersed on the surface of a support and may constitute no more than about 1% of the total catalyst. The main reason for dispersing the catalytic species is the expense. The expensive material must be accessible to reactants, and this requires that most of the catalytic material be present at a surface. This is possible only if the material is dispersed as minute particles, as small as 1 nm in diameter and even less. It is not practical to use minute

particles by themselves, as they would be entrained in products and clog lines and pumps, and their use in a fixed-bed reactor would cause large pressure drops. Dispersion on a support may also help stabilize the catalytically active species.

Supports. The principal component of a typical catalyst is the porous support (49,50). Most supports are robust solids that can be made with wide ranges of surface areas and pore size distributions. The most widely applied supports are metal oxides; others are carbon, kieselguhr, organic polymers, and zeolites.

The most commonly applied catalyst support is γ - Al_2O_3 , one of the transition aluminas (51,26). These are defective metastable solids formed from $\text{Al}(\text{OH})_3$ by heating it to about 500°C or more (51); continued heating gives the more stable δ - Al_2O_3 . As the $\text{Al}(\text{OH})_3$ is heated in air, it decomposes into an oxide with a micropore system and a surface area of hundreds of square meters per gram. The solid consists of small, crystalline primary particles; the spaces between these primary particles are micropores and mesopores. As the solid is heated to about 1100°C , there is a series of phase changes and ultimately a collapse of the pore structure and loss of almost all the internal surface area as finally the extremely hard, crystalline α - Al_2O_3 (corundum) is formed. It has a melting point of about 2100°C (see ALUMINUM COMPOUNDS, ALUMINUM OXIDE (ALUMINA)).

Transition aluminas are good catalyst supports because they are inexpensive and have good physical properties. They are mechanically stable, stable at relatively high temperatures even under hydrothermal conditions, ie, in the presence of steam, and easily formed in processes such as extrusion into shapes that have good physical strength such as cylinders. Transition aluminas can be prepared with a wide range of surface areas, pore volumes, and pore size distributions.

Macropores can be introduced into γ - Al_2O_3 by including particles of an organic material such as carbon or sawdust with the $\text{Al}(\text{OH})_3$ (51). When the γ - Al_2O_3 is formed, the organic particles are surrounded by the alumina. The organic material is removed by burning, leaving macropores; the macropore dimensions are determined by the particle size of the organic material.

Most catalyst supports are simply nearly inert platforms that help stabilize the dispersion of the catalytically active phase. Sometimes, however, the supports play a direct catalytic role, as exemplified by the alumina used in supported Pt and RePt catalysts for naphtha reforming.

The surfaces of γ - Al_2O_3 and most other metal oxides are covered with polar functional groups including OH groups and O^{2-} ions (52). A structural model of γ - Al_2O_3 is shown in Figure 11 (53). When the solid is heated, it gives off water in a reversible process called dehydroxylation (54). As a result, surface OH groups are lost and Al^{3+} ions are exposed at the surface. The microparticles of the oxide interact strongly with each other through the surface functional groups; for example, hydrogen bonding can occur. As a result, a microporous solid consisting of such particles is a strong material. In contrast, some support materials, exemplified by α - Al_2O_3 , have few surface functional groups, and a solid consisting of microparticles of such a material lacks physical strength.

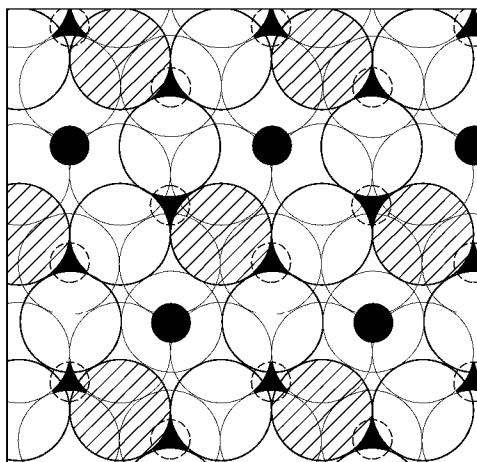


Fig. 11. Structural model of the (111) face of γ -alumina (53). The small solid circles represent Al^{3+} , the large open circles OH groups, and the hatched circles oxygen. The surface is 50% dehydroxylated.

Binders. To create needed physical strength in catalysts, materials called binders are added (51); they bond the catalyst. A common binder material is a clay mineral such as kaolinite. The clay is added to the mixture of microparticles as they are formed into the desired particle shape, for example, by extrusion. Then the support is heated to remove water and possibly burnout material and then subjected to a high temperature, possibly 1500°C , to cause vitrification of the clay; this is a conversion of the clay into a glasslike form that spreads over the microparticles of the support and binds them together.

Promoters. Many industrial catalysts contain promoters, commonly chemical promoters. A chemical promoter is used in a small amount and influences the surface chemistry. Alkali metals are often used as chemical promoters, for example, in ammonia synthesis catalysts, ethylene oxide catalysts, and Fischer-Tropsch catalysts (55). They may be used in as little as parts per million quantities. The mechanisms of their action are usually not well understood. In contrast, seldom-used textural promoters, also called structural promoters, are used in massive amounts and affect the physical properties of the catalyst. These are used in ammonia synthesis catalysts.

CATALYST TREATMENTS

Catalysts often require activation or regeneration and their disposal also requires special consideration (56).

Activation. Some catalysts, eg, Ziegler olefin polymerization catalysts (57), are highly reactive in the presence of air, and some, eg, iron catalysts, are even pyrophoric; these must be handled under a blanket of inert gas. The surfaces of most catalysts are reactive and not easily maintained in an active state in the form in which they are conveniently supplied. Thus many catalysts must be activated prior to use. The activation may be as simple as exposure to reactants under processing conditions, but some catalysts require specialized treatments. For example, catalysts used for hydroprocessing of fossil fuels are usually delivered as supported metal oxides, but in the operating state they are supported metal sulfides. Catalyst suppliers specify detailed procedures for treatment, eg, with a mixture of hydrogen and oil containing organosulfur compounds, to carry out the sulfiding properly. The details are often critical, and the catalyst manufacturer's guarantees may be void if the procedure is not carried out properly.

Deactivation. Catalysts lose activity and selectivity in many ways, and much effort in process development goes into measuring the deactivation and finding means to minimize it. Some catalysts undergo physical changes during normal operation; for example, a catalytically active phase may be transformed into an inactive phase. Catalysts also undergo sintering, which is a coalescence of particles to give larger particles, accompanied by loss of surface area. Iron sinters under conditions of ammonia synthesis, but when a textural promoter such as alumina is present, the sintering is greatly reduced. Catalyst components may be volatile and gradually vaporized during use; examples are silica used as a support and molybdenum oxides present in selective oxidation catalysts.

Catalysts commonly lose activity in operation as a result of accumulation of materials from the reactant stream. Catalyst poisoning is a chemical phenomenon. A catalyst poison is a component such as a feed impurity that as a result of chemisorption, even in small amounts, causes the catalyst to lose a substantial fraction of its activity. For example, sulfur compounds in trace amounts poison metal catalysts. Arsenic and phosphorus compounds are also poisons for a number of catalysts. Sometimes the catalyst surface has such a strong affinity for a poison that it scavenges it with a high efficiency. The

poison may then adsorb strongly on the catalyst at the upstream end of a fixed-bed reactor at the beginning of operation, with a wave then moving downstream through the reactor as the upstream surface becomes saturated.

A selective poison is one that binds to the catalyst surface in such a way that it blocks the catalytic sites for one kind of reaction but not those for another. Selective poisons are used to control the selectivity of a catalyst. For example, nickel catalysts supported on alumina are used for selective removal of acetylene impurities in olefin streams (58). The catalyst is treated with a continuous feed stream containing sulfur to poison it to an exactly controlled degree that does not affect the activity for conversion of acetylene to ethylene but does poison the activity for ethylene hydrogenation to ethane. Thus the acetylene is removed and the valuable olefin is not converted.

Because catalyst surfaces are reactive and often sensitive to their environments, they may be irreversibly changed by exposure to undesired reactants. Upsets in plant operations can lead to catastrophic losses of whole catalyst charges. A large catalyst charge that is ruined can cost hundreds of thousands of dollars as well as the cost of lost operation.

Catalysts are also deactivated or fouled by physical deposition of materials present in or formed from feeds. Sometimes massive deposits form on surfaces and block access of reactants to the catalytic sites. Coke is carbonaceous material of various compositions, often aromatic and with a high molecular weight and a typical composition of approximately CH. Coke forms on every hydrocarbon processing catalyst and on most catalysts used for organic chemical conversions. Inorganic materials are also deposited on catalysts. For example, the organovanadium and organonickel compounds in petroleum residua react to form vanadium and nickel sulfides on the surfaces of hydroprocessing catalysts. The solid deposits reduce activity by covering catalytic sites, filling pores, and restricting the entry of reactants. When the effectiveness factor for the deposition reaction is small, the pore mouths can become blocked and catalysts can suffer near catastrophic failure. Small particles of solid such as dust can also foul catalysts. This may be a problem in processes for cleanup of NO_x emissions from coal-fired power plants, and catalysts are designed in the form of monoliths (honeycombs) to minimize the effect.

Regeneration. Deactivated catalysts are treated to bring back the catalytic activity in processes called regenerations. Coke deposits are removed by controlled combustion. Often low partial pressures of oxygen are used to keep the rate of combustion and the temperature rise from becoming too large and leading to damage of the catalyst, such as by sintering. Periodic coke burn-off can be carried out many times with little damage to many catalysts. Catalysts used for cracking of petroleum are in contact with reactants for only a few seconds; they are separated and flow to another reactor where they are regenerated, but most catalysts last for months or years between regenerations (see CATALYSTS, REGENERATION).

Redispersion. Expensive catalyst components such as precious metals are used in high dispersions on supports. During operation, the small metal particles tend to sinter, ie, migrate and agglomerate, into larger particles with a loss of metal surface area and thereby a loss of catalytic activity. The metals in such catalysts may be redispersed as part of the catalyst regeneration (59). For example, after the coke is burned off a supported platinum catalyst, the catalyst may be treated with a reactive atmosphere containing chlorine and oxygen to form volatile platinum oxychloride species that are transported through the gas phase and deposited on the pore walls, where they are then treated in H₂ and reduced. The result is an increased dispersion of the platinum and a reactivated catalyst.

Reclamation, Disposal, and Toxicity. Removal of poisons and inorganic deposits from used catalysts is typically difficult and usually uneconomical. Thus some catalysts are used without regeneration, although they may be processed to reclaim expensive metal components. Used precious metal catalysts, including automobile exhaust conversion catalysts, are treated (often by the suppliers) to extract the metals, and recovery efficiencies are high. Some spent hydroprocessing catalysts may be used as sources of molybdenum and other valuable metals.

Some catalysts are hazardous materials, or they react to form hazardous substances. For example, catalysts used for hydrogenation of carbon monoxide form volatile metal carbonyl compounds such as nickel carbonyl, which are highly toxic. Many catalysts contain heavy metals and other hazardous components, and environmentally safe disposal has become an increasing concern and expense.

CATALYST PREPARATION

Catalyst preparation is more an art than a science. Many reported catalyst preparations omit important details and are difficult to reproduce exactly, and this has hindered the development of catalysis as a quantitative science. However, the art is developing into a science and there are now many examples of catalysts synthesized in various laboratories that have nearly the same physical and catalytic properties.

Supports are often prepared first and the catalyst and promoter components added later (60). Metal oxide supports are usually prepared by precipitation from aqueous solutions. Nitrates are commonly used anions; alkalies and ammonium are commonly used cations. Metal oxide supports, eg, silica and alumina, are prepared in the form of hydrogels. Mixed oxides such as silica–alumina are made by cogelation. Careful control of conditions such as pH is important to give uniform products.

Supports are washed at controlled values of pH to remove impurities. Ions and impurities in the preparative solution are easily occluded in the solid and difficult to remove by washing. Therefore, ions that might poison the catalyst, eg, Cl⁻, SO₄²⁻, or alkali metal ions, are avoided. Many of the materials are cation exchangers, and washing does not remove cations from them. Metal ions can be removed by exchange with ammonium ions, which on heating give off ammonia and leave hydrogen ions in surface —OH groups. Drying of precipitates and hydrated gels leads to evolution of gases and may generate microporosity, as described above for transition aluminas. Porosity can also be created by reduction of a nonporous oxide; porous iron can be made this way.

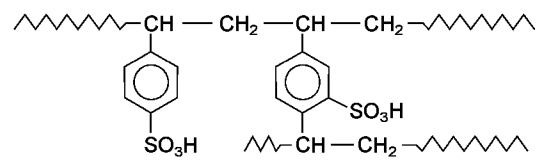
Catalyst components are usually added in the form of precursor metal salts in aqueous solutions. In impregnation, the support may be dried, evacuated, and brought in contact with an excess of an impregnating solution containing metal salts. The solid is then dried and calcined, ie, brought to a high temperature, usually in air. Alternatively, in the incipient wetness method, just enough of the impregnating solution is used to fill the pores of the support. The chemistry of the interactions of catalyst precursors with metal oxide supports is beginning to be understood. Important parameters that control the adsorption of metal complex precursors from aqueous solution are the isoelectric point of the metal oxide, the pH of the solution, and the nature of the metal complex (61). Depending on the conditions of the contact, cationic or anionic species may be adsorbed. Sometimes these are simple mononuclear (single-metal atom) species, but sometimes they are complicated polynuclear ions. The nature of the initially adsorbed species may significantly affect the structure of the catalytic species in the resultant catalyst. After impregnation, the catalyst may be activated, for example, by drying and calcining. Promoters may be added at various stages, for example, as a final step in the preparation or just prior to operation.

Supported metal catalysts are reduced, for example, by treatment in hydrogen at temperatures in the range of 300–500°C. The reduction temperature may influence the stability of the metal dispersion.

EXAMPLES OF SURFACE CATALYSIS

Molecular Catalysis on Supports. The term molecular catalysis is commonly applied only to reactions in uniform fluid phases, but it applies nearly as well to some reactions taking place on supports. Straightforward examples are reactions catalyzed by polymers functionalized with groups that closely resemble catalytic groups in solution. Industrial examples include reactions catalyzed by ion-exchange resins, usually sulfonated poly(styrene–divinylbenzene) (62). This polymer is an industrial catalyst for synthesis of methyl *t*-butyl ether (MTBE) from methanol and isobutylene and synthesis of bisphenol A from phenol and acetone, among others. The former application has grown rapidly as MTBE has become a component of high octane number gasoline (see ETHERS).

The polymer has the following structure, which is shown schematically.

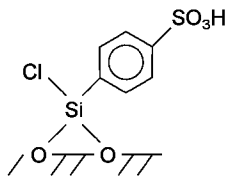


The sulfonated resin is a close analogue of *p*-toluenesulfonic acid in terms of structure and catalyst performance. In the presence of excess water, the SO₃H groups are dissociated, and specific acid catalysis takes place in the swelled resin just as it takes place in an aqueous solution. When the catalyst is used with weakly polar reactants or with concentrations of polar reactants that are too low to cause dissociation of the acid groups, general acid catalysis prevails and water is a strong reaction inhibitor (63).

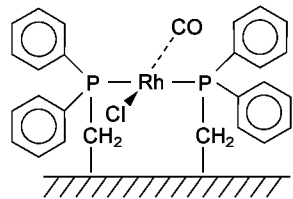
The polymer-supported catalysts are thus important conceptually in linking catalysis in solutions and catalysis on supports. The acid–base chemistry is fundamentally the same whether the catalytic groups are present in a solution or anchored to the support. The polymer-supported catalysts have replaced acid solutions in numerous processes because they minimize the corrosion, separation, and disposal problems posed by mineral acids.

Polymer-supported catalysts incorporating organometallic complexes also behave in much the same way as their soluble analogues (28). Extensive research has been done in attempts to develop supported rhodium complex catalysts for olefin hydroformylation and methanol carbonylation, but the effort has not been commercially successful. The difficulty is that the polymer-supported catalysts are not sufficiently stable; the valuable metal is continuously leached into the product stream (28). Consequently, the solid catalysts fail to eliminate the problems of corrosion and catalyst recovery and recycle that are characteristic of solution catalysis.

Surfaces of inorganic solids can be functionalized with catalytic groups just as organic polymers can. For example, the hydroxyl groups on the surface of silica can be used for synthesis of the following structure:



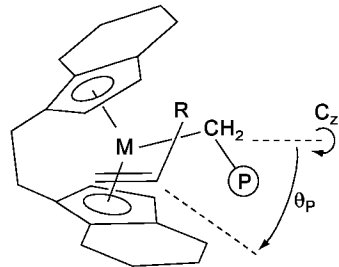
This is an ion-exchanger like the sulfonated polymer. The silica surface can also be functionalized with phosphine complexes; when combined with rhodium, these give anchored complexes that behave like their soluble and polymer-supported analogues as catalysts for olefin hydrogenation and other reactions:



These silica-supported catalysts demonstrate the close connections between catalysis in solutions and catalysis on surfaces, but they are not industrial catalysts. However, silica is used as a support for chromium complexes, formed either from chromocene or chromium salts, that are industrial catalysts for polymerization of α -olefins (64,65). Supported chromium complex catalysts are used on an enormous scale in the manufacture of linear polyethylene in the Unipol and Phillips processes (see [OLEFIN POLYMERS](#)). The exact structures of the surface species are still not known, but it is evident that there is a close analogy linking soluble and supported metal complex catalysts for olefin polymerization.

This conceptual link extends to surfaces that are not so obviously similar in structure to molecular species. For example, the early Ziegler catalysts for polymerization of propylene were α -TiCl₃. Today, supported Ti complexes are used instead (26,57). These catalysts are selective for stereospecific polymerization, giving high yields of isotactic polypropylene from propylene. The catalytic sites are believed to be located at the edges of TiCl₃ crystals. The surface structures have been inferred to incorporate anion vacancies; that is, sites where Cl⁻ ions are not present and where Ti³⁺ ions are exposed (66). These cations exist in octahedral surroundings. The polymerization has been explained by a mechanism whereby the growing polymer chain and an adsorbed propylene bonded cis to it on the surface undergo an insertion reaction (67). In this respect, there is no essential difference between the explanation of the surface catalyzed polymerization and that catalyzed in solution.

The occurrence of stereospecific polymerization in solution has been explained by the steric restrictions of ligands bonded to the metal center. For example, the following structure has been postulated as an intermediate in solution catalysis (68):



The steric constraints imposed by the bulky ligands cause the propylene to bond almost entirely with a single orientation with respect to the growing polymer chain, CH₂-**(P)**, which leads to the stereoregular product.

The explanation for the stereospecificity of the surface catalysis, which preceded that for the solution catalysis, is based on the structure inferred for the α -TiCl₃ crystal edges; the locations of the Cl⁻ ions at the anion vacancies create an unsymmetrical environment whereby the growing polymer chain and the adsorbed propylene are oriented predominantly in a single, energetically favored way that leads to the stereoregular polymer as a result of a series of insertion reactions (67). The explanation is simplified and the details are not fully understood, but again there is a strong conceptual link between molecular and surface catalysis. It is difficult to forge many such links because of the lack of detailed understanding of most surface catalyzed reactions, which is a consequence of the complexity of the surface compositions and structures of solid catalysts.

Catalysis by Metals. Metals are among the most important and widely used industrial catalysts (69,70). They offer activities for a wide variety of reactions (Table 1). Atoms at the surfaces of bulk metals have reactivities and catalytic properties different from those of metals in metal complexes because they have different ligand surroundings. The surrounding bulk stabilizes surface metal atoms in a coordinatively unsaturated state that allows bonding of reactants. Thus metal surfaces offer an advantage over metal complexes, in which there is only restricted stabilization of coordinative

unsaturation. Furthermore, metal surfaces provide catalytically active sites that are stable at high temperatures. For example, supported palladium catalysts have replaced soluble palladium for vinyl acetate synthesis; the advantages of the solid include reduced corrosion and reduced formation of by-products.

CO Oxidation Catalyzed by Palladium. One of the best understood catalytic reactions occurring on a metal surface is the oxidation of carbon monoxide on palladium:



This reaction takes place similarly in automobile exhaust converters, although the metals in these catalysts are platinum and rhodium, among other components, and other reactions occur.

CO oxidation catalysis is understood in depth because potential surface contaminants such as carbon or sulfur are burned off under reaction conditions and because the rate of CO oxidation is almost independent of pressure over a wide range. Thus ultrahigh vacuum surface science experiments could be done in conjunction with measurements of reaction kinetics (71). The results show that at very low surface coverages, both reactants are adsorbed randomly on the surface; CO is adsorbed intact and O₂ is dissociated and adsorbed atomically. When the coverage by CO is more than 1/3 of a monolayer, chemisorption of oxygen is blocked. When CO is adsorbed at somewhat less than a monolayer, oxygen is adsorbed, and the two are present in separate domains. The reaction that forms CO₂ on the surface then takes place at the domain boundaries.

The available results are consistent with the following sequence of steps on the surface (71):



This depiction is vague because the exact nature of the sites and their bonding with reactants are not known. The experimental results have led to an approximate potential energy diagram characterizing these elementary steps on the surface (Fig. 12) (71). This shows the role of the surface in providing an efficient pathway for the reaction. Most of the energy is liberated as the reactants are adsorbed; the activation energy for reaction of the adsorbed CO with the adsorbed O is relatively small, and this step is only slightly exothermic.

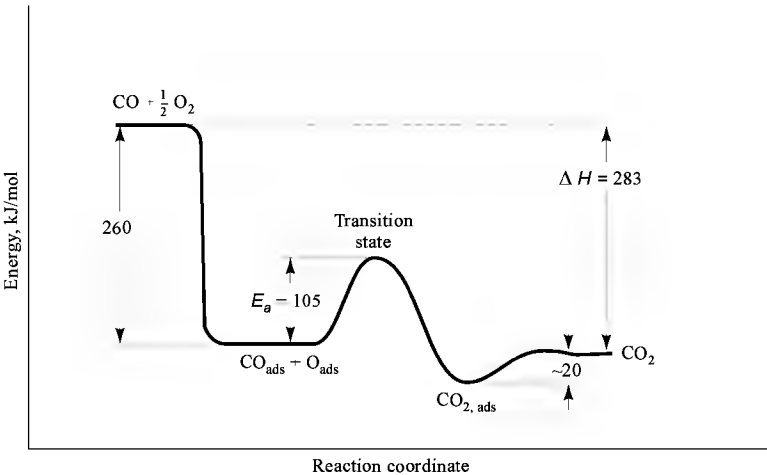


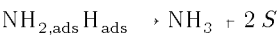
Fig. 12. Schematic potential energy diagram illustrating the changes associated with the individual reaction steps in CO oxidation on Pd (71). $E_a = 105\text{ kJ/mol}$; $\Delta H = 283\text{ kJ/mol}$. To convert kJ to kcal, divide by 4.184.

Ammonia Synthesis. Another well-understood reaction is the ammonia synthesis:



This reaction is catalyzed by iron, and extensive research, including surface science experiments, has led to an understanding of many of the details (72). The adsorption of H₂ on iron is fast, and the adsorption of N₂ is slow and characterized by a substantial activation energy. N₂ and H₂ are both dissociatively adsorbed. Adsorption of N₂ leads to reconstruction of the iron surface and formation of structures called iron nitrides that have depths of several atomic layers with compositions of approximately Fe₄N. There is a bulk compound Fe₄N, but it is thermodynamically unstable when the surface structure is stable. Adsorbed species such as the intermediates NH and NH₂ have been identified spectroscopically.

The following sequence of steps explains the observations (72):



(30)

where *S* refers to surface sites, the exact nature of which is unknown. An approximate potential energy diagram for this sequence of steps is shown in Figure 13, which shows how the catalyst facilitates the bond breaking reactions. The energy gain resulting from the formation of the strong metal–nitrogen and metal–hydrogen bonds makes the first steps endothermic. The dissociative adsorption of N₂ is rate determining, not because of a high activation energy barrier but because the frequency factor, preexponential factor, in the rate constant is small. The ammonia synthesis mechanism is so well understood that rates of the reaction under practical conditions have been predicted from the rate of adsorption of N₂ measured under low pressure conditions, far from those of practical catalysis, combined with the equilibria of the other steps (73). The prediction was within a factor of two of the observed rate of the industrial reaction. This result is a satisfying consolidation of decades of fundamental research motivated by an important catalytic process.

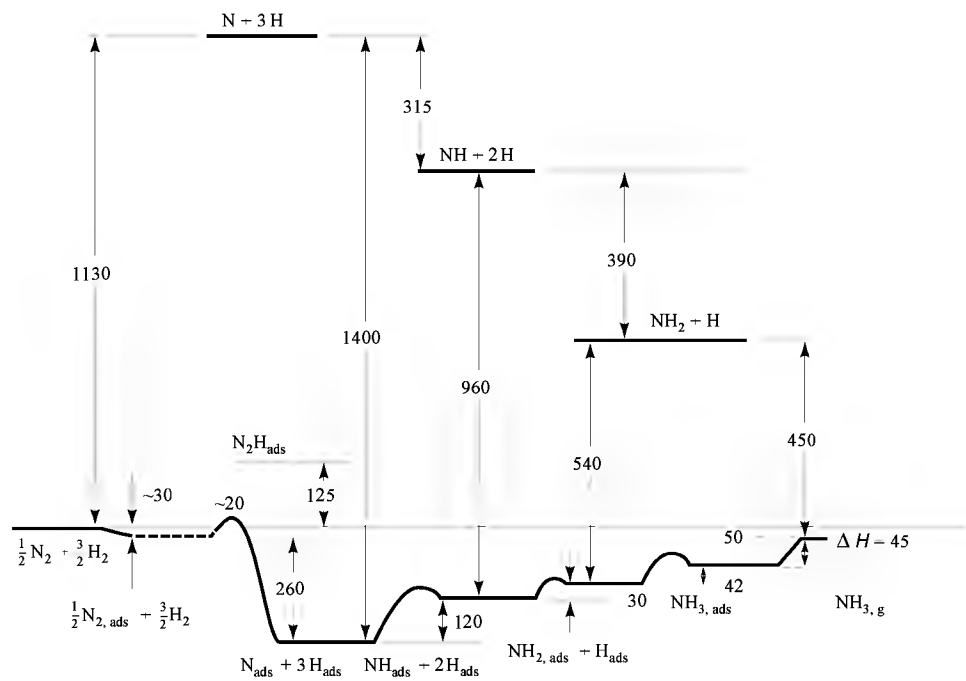


Fig. 13. Schematic potential energy diagram for the catalytic synthesis and decomposition of ammonia on iron. The energies are given in kJ / mol; to convert to kcal, divide by 4.184 (72).

The industrial catalysts for ammonia synthesis consist of far more than the catalytically active iron (74). There are textural promoters, alumina and calcium oxide, that minimize sintering of the iron and a chemical promoter, potassium (about 1 wt % of the catalyst), and possibly present as K₂O; the potassium is believed to be present on the iron surface and to donate electrons to the iron, increasing its activity for the dissociative adsorption of N₂. The primary iron particles are about 30 nm in size, and the surface area is about 15 m² / g. These catalysts last for years.

Catalysis by Metal Oxides and Zeolites. Metal oxides are common catalyst supports and catalysts. Some metal oxides alone are industrial catalysts; an example is the γ-Al₂O₃ used for ethanol dehydration to give ethylene. But these simple oxides are the exception; mixed metal oxides are more common. For example, silica–alumina was used earlier as a catalyst for cracking of petroleum and is still a component of such catalysts, and bismuth molybdates were used for ammoxidation of propylene to give acrylonitrile. Metal oxides supported on metal oxides are also commonly applied. For example, rhenium oxide, Re₂O₇, supported on alumina is used for olefin metathesis (30), and complicated supported oxides related to bismuth molybdates are used for ammoxidation.

Metal oxide surfaces are more complex in structure and composition than metal surfaces, and they are not so easy to characterize with some ultrahigh vacuum techniques, eg, electron spectroscopies, because they are poor electrical conductors and build up electrical charge when subjected to streams of charged particles. Consequently, understanding of catalysis on metal oxide surfaces is less advanced than understanding of catalysis on metal surfaces, although significant progress has been made (75,76).

Acid–base chemistry of metal oxide surfaces is important in catalysis and is characterized by measurements such as infrared spectroscopy with adsorbed probe molecules, eg, the base pyridine. The surfaces have both basic and acidic character. OH and O groups have base strengths ranging from weak, eg, in silica gel, to moderate, eg, in γ-Al₂O₃, to strong, eg, in highly dehydroxylated MgO. Surface OH groups are acids with proton donor strengths ranging from weak, eg, in Al₂O₃, to strong, eg, in SiO₂–Al₂O₃. Metal ions exposed at surfaces are Lewis acids. Redox properties are also important in some catalytic applications, as cations in some oxides, eg, V₂O₅, can change oxidation state. And the principles of organometallic chemistry are useful in describing the interactions of organic ligands with metal ions exposed at surfaces.

Zeolites and Catalytic Cracking. The best-understood metal oxide catalysts are zeolites, ie, crystalline aluminosilicates (77–79). The zeolites are well understood because they have much more nearly uniform compositions and structures than amorphous metal oxides such as silica and alumina. Here the usage of amorphous refers to results of x-ray diffraction experiments; the crystallites of a metal oxide such as γ-Al₂O₃ that constitute the microparticles are usually so small that sharp x-ray diffraction patterns are not measured; consequently the solids are said to be x-ray amorphous or simply amorphous.

Zeolites contain Si, Al, and O ions and various other cations. The structures are built up of linked SiO₄ and AlO₄ tetrahedra that share O ions. These tetrahedra are arranged in a number of ways to give the different zeolites. The structures are unique in that they incorporate pores as part of the regular crystalline structures. The pores have dimensions of the order of molecular dimensions so that some molecules fit into the pores and some do not. Hence the zeolites are molecular sieves (qv), and they are applied in industrial separations processes to take advantage of this property. Some zeolites and their pore dimensions are listed in Table 2.

Table 2. Zeolites and Their Pore (Aperture) Dimensions^a

Zeolite	CAS Registry Number	Number of oxygens in the ring	10 × Aperture dimensions, nm
chabazite	[12251-32-0]	8	3.6 × 3.7
erionite	[12510-42-8]	8	3.6 × 5.2

zeolite A		8	4.1
ZSM-5 (or silicalite)	[58339-99-4]	10	5.1 × 5.5; 5.4 × 5.6
ZSM-11		10	5.1 × 5.5
heulandite		10	4.4 × 7.2
ferrierite ^b		10	4.3 × 5.5
faujasite	[12173-28-2]	12	7.4
zeolite L		12	7.1
mordenite	[12173-98-7]	12	6.7 × 7.0
offretite		12	6.4

^a The framework oxygen is assumed to have a diameter of 0.275 nm.
^b There are also apertures with eight-membered oxygen rings in this zeolite.

A catalytically important family of zeolites called faujasites (zeolites X and Y) is represented in Figure 14. Here the points of intersection of the lines represent Si or Al ions; oxygen is present at the center of each line. This depiction emphasizes the framework structure of the zeolite and shows the presence of the intracrystalline pore structure in which there are spaces called supercages, each with a diameter of about 1.2 nm. The pore structure is three dimensional; the supercages are connected by apertures with diameters of about 0.74 nm. Some rather large molecules can fit through these apertures (Fig. 15) (80) and undergo catalytic reaction in the cages.

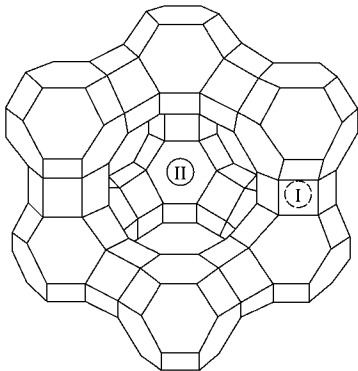


Fig. 14. Schematic representation of the structure of a faujasitic zeolite. I and II indicate cation positions.

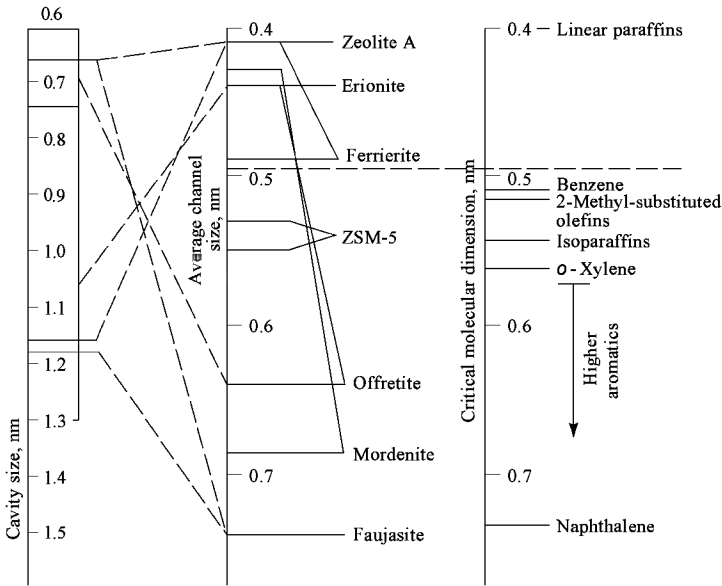
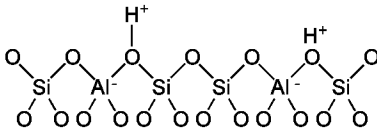


Fig. 15. Pore dimensions of zeolites and critical dimensions of hydrocarbons (80).

The zeolite frame is made up of SiO₄ tetrahedra, which are neutral, and AlO₄ tetrahedra, which have a charge of -1. The charge of the AlO₄ tetrahedra is balanced by the charges of additional cations that exist at various crystallographically defined positions in the zeolite, many exposed at the internal surface. Zeolites are thus ion exchangers. The cations may be catalytically active. When the cations are H⁺, the zeolites are acidic. Acidic zeolite Y finds enormous industrial application as a component of petroleum cracking catalysts. In the following simplified structure, the OH groups located near AlO₄ tetrahedra are strong Brunnsted acids and responsible for the catalytic activity for many reactions:



Zeolites are named to represent the exchangeable cations in them; for example, NaY is zeolite Y with sodium ions in the cation exchange positions. Another catalytically important zeolite is ZSM-5 (81). There is a three-dimensional network of pores in this zeolite, represented in Figure 16. A set of straight parallel pores is intersected by a set of perpendicular zigzag pores. These pores are smaller than those of the faujasites (Fig. 15). ZSM-5 is classified as a medium pore zeolite, the faujasites are large pore zeolites, and zeolite A (Table 2) is a small pore zeolite.

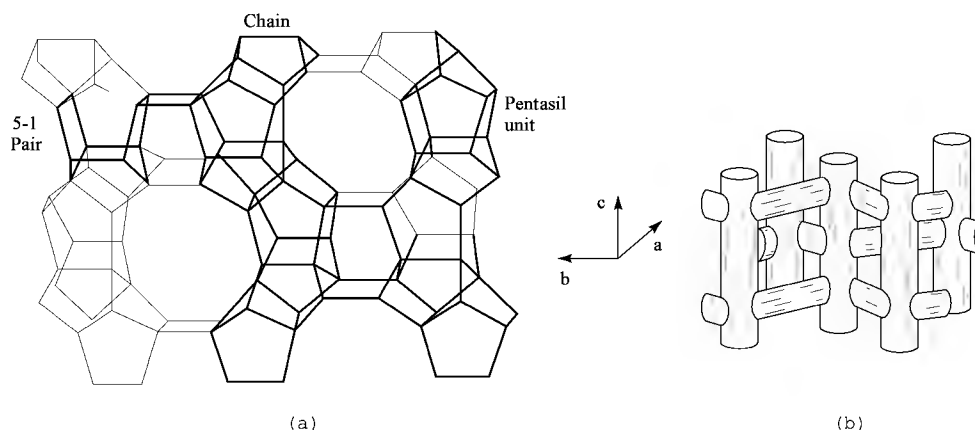


Fig. 16. Structure of the zeolite ZSM-5 (81): (a) framework of the zeolite; (b) schematic representation of the pore structure.

Both the faujasites and ZSM-5 in the acidic form catalyze many reactions that are catalyzed by other soluble and solid acids. The zeolites are not very strong acids at low temperatures, but at 500°C they are such strong acids that they can protonate paraffins; thus they are superacids. Almost all the catalytic applications of zeolites take advantage of their acidic properties. Activities of a family of HZSM-5 samples with different Si: Al ratios have been studied (82). When the Al contents are low, the catalytic activity is proportional to the Al content of the zeolite over a wide range of compositions. These results identify the proton donor sites associated with the Al cations as the catalytic sites for the cracking reaction. At higher concentrations of Al in the zeolite, the dependence is no longer linear.

ZSM-5 is a component of some catalysts for cracking of petroleum, but the larger pored zeolite Y in an acidic form is the principal catalytic component. Zeolite Y is sometimes used in a form containing hydrogen ions to provide acidity and rare-earth ions such as La^{3+} , which make the structure more stable. The stability is valuable because the zeolites are deactivated in a matter of a few seconds of contact with reactant vapors in the catalytic reactor and are subjected to an atmosphere of oxygen and steam at temperatures as high as about 800°C in the regenerator where coke is burned off.

The feedstocks to crackers are petroleum fractions ranging from gas oil to residuum. They undergo a complicated set of reactions, including cracking, isomerization, disproportionation, and coke formation, that proceed through carbenium ion intermediates and give predominantly lower molecular weight products, including, for example, many in the gasoline boiling range (83,84). The patterns in the chemistry of catalytic cracking are consistent with the chemistry of hydrocarbons and carbenium ions in solution at much lower temperatures. For example, cracking of a paraffin takes place in a cycle that is initiated by formation of a carbenium ion by protonation of an olefin by the catalyst. The chain reaction is the following:



The second step is a β -scission, the breaking of a carbon-carbon bond β to the charged carbon. The sum of the two reactions is the stoichiometry of the overall cracking reaction $\text{R}'\text{H} \rightarrow \text{RH} + \text{olefin}$. R^+ , a relatively stable carbenium ion such as the *t*-butyl cation, is a chain carrier. The role of the catalyst is to donate the proton to start the chain. This is a greatly simplified representation.

Cracking catalysts are complex composites consisting of a support, eg, silica-alumina, and the catalytically active zeolite, present as crystallites roughly 1 μm in size dispersed in a matrix of the amorphous support (83). The catalyst particles are small, roughly 50 μm in diameter on average so that they can be fluidized by the vaporized oil entering the cracking reactor. The reactant vapors carry the catalyst particles with them; such a design is necessary because the catalyst is largely deactivated by coke after only several seconds of operation and must therefore be efficiently transported out of the reactor and into the regenerator where the coke is burned off.

The catalyst may contain about 20 wt % zeolite, and more or less is used, depending on the feedstock and operating goals. The principal component of the catalyst is the matrix, which has a relatively low catalytic activity, but it is active for cracking the molecules that are too large to fit into the zeolite pores. The matrix also plays the role of a heat-transfer medium; the cracking reactions are fast and endothermic, and the temperature of the catalyst and the rates of the reactions fall as the catalyst is carried by the oil vapors from the inlet toward the outlet of the reactor. The thermal mass of the matrix keeps the temperature drop from being too large and causing the cracking rate to fall off too quickly. After leaving the reactor, the catalyst is heated up in the regenerator where the coke is burned off and reenters the reactor at a suitably high temperature.

In addition to the matrix and the catalytically active zeolite there are small amounts of a supported metal such as platinum on alumina, which catalyzes CO oxidation in the regenerator and minimizes the emissions of CO. There are also metal oxide components that minimize the emission of SO_x formed in the regenerator from combustion of organosulfur compounds from the oil. The metal oxides react with SO_x in the regenerator to make stable metal sulfates. Cycled with the regenerated catalyst to the reducing atmosphere of the cracking reactor, the sulfates are converted into H_2S , which is removed by scrubbing the effluent gas stream.

There are numerous structures that are similar to zeolites, such as aluminophosphate molecular sieves, AlPOs, but these have not found catalytic applications. Zeolites can be modified by incorporation of cations in the crystalline lattice which are not exchangeable ions, but can play catalytic roles. For example, silicalite, which has the structure of ZSM-5 but without Al, incorporating Ti in the lattice is a commercial catalyst for oxidation of phenol with H_2O_2 to give diphenols; the catalytic sites may be isolated Ti cations (85).

Shape-Selective Catalysis. The zeolites are unique in their molecular-sieving character, which is a consequence of their narrow, uniform pores (86). The transport of molecules in such small pores is different from that in the larger pores of typical catalysts. Figure 17 is a schematic representation of the diffusion coefficients of molecules in pores (87). When the pore diameters are large in comparison with the dimensions of the diffusing molecules, then molecular diffusion occurs, as it does in a fluid phase. When the pores become smaller, the interactions of the molecules with the pore walls become dominant, and Knudsen diffusion occurs. When the pores become so small that the molecules barely fit through them, then configurational diffusion occurs. This diffusion may be characterized by a substantial activation energy; the rate of diffusion is a strong function of the pore and molecule sizes in this regime. In the limit, a pore is too small for a molecule to fit in, and the diffusion coefficient becomes zero.

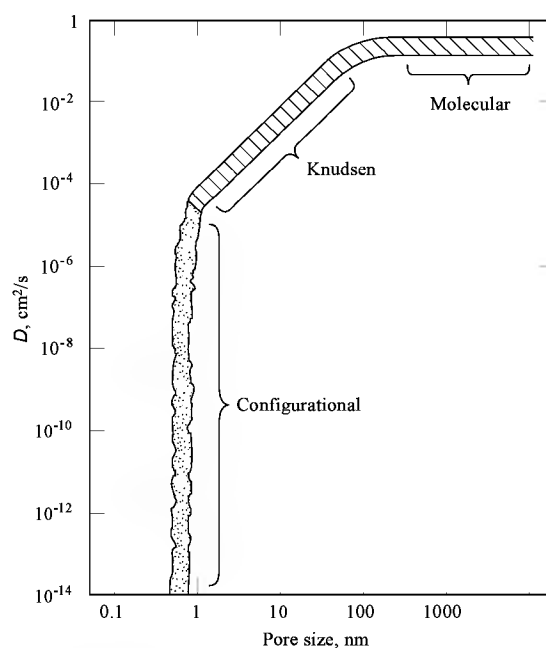


Fig. 17. Schematic representation of the regimes of diffusion in pores (87).

Catalytic processes have been developed to take advantage of the unique transport and molecular sieving properties of zeolites. The zeolite that has found the most applications is the medium-pored HZSM-5 (86). The term shape-selective catalysis is applied to describe the unique effects. There are different kinds of shape selectivity. Mass transport selectivity is a consequence of transport restrictions whereby some species diffuse more rapidly than others in the zeolite pores. In the simplest kind of shape-selective catalysis, small molecules in a mixture enter the pores and are catalytically converted whereas large molecules pass through the reactor unconverted because they do not fit into the pores where the catalytic sites are located. This statement is slightly oversimplified as there are a few catalytic sites on the outer surfaces of zeolite crystallites. Similarly, product molecules formed inside a zeolite may be so large that their transport out of the zeolite may be very slow, and they may be converted largely into other products that diffuse more rapidly into the product stream. A different kind of shape selectivity is called restricted transition state selectivity (86). It is not related to transport restrictions; rather, it is related to the size restriction of the catalyst pore that suppresses the formation of the transition state for a certain reaction, whereas it may not suppress the formation of a smaller transition state for another reaction. A way to diagnose the nature of the shape selectivity is to use zeolite crystallites of various sizes as the catalyst. Mass transport selectivity is influenced by the particle size; restricted transition state selectivity is not.

For example, HZSM-5 is a component of some cracking catalysts. It selectively cracks the straight-chain paraffins rather than the branched paraffins because of a restricted transition state selectivity effect. This is a desired processing goal as the straight-chain isomers have lower octane numbers than the others and are less desirable gasoline components. In this example, the catalyst favors the reaction of the straight-chain compounds, even though they are intrinsically less reactive because they initially form secondary rather than the more stable and easily formed tertiary carbenium ions. Thus the pore size restriction reverses the pattern of selectivity that would be expected on the basis of the intrinsic chemistry alone.

Mass transport selectivity is illustrated by a process for disproportionation of toluene catalyzed by HZSM-5 (86). The desired product is *p*-xylene; the other isomers are less valuable. The ortho and meta isomers are bulkier than the para isomer and diffuse less readily in the zeolite pores. This transport restriction favors their conversion to the desired product in the catalyst pores; the desired para isomer is formed in excess of the equilibrium concentration. Xylene isomerization is another reaction catalyzed by HZSM-5, and the catalyst is preferred because of restricted transition state selectivity (86). An undesired side reaction, the xylene disproportionation to give toluene and trimethylbenzenes, is suppressed because it is bimolecular and the bulky transition state cannot readily form.

Mixed Metal Oxides and Propylene Ammoxidation. The best catalysts for partial oxidation are metal oxides, usually mixed metal oxides. For example, phosphorus–vanadium oxides are used commercially for oxidation of *n*-butane to give maleic anhydride, and oxides of bismuth and molybdenum with other components are used commercially for oxidation of propylene to give acrolein or acrylonitrile.

The surface of a mixed metal oxide exposes two kinds of metal ions in addition to O^{2-} ions and OH groups. Selective oxidation of hydrocarbons, represented schematically in Figure 18 (10), takes place on surface sites having oxygen atoms of limited reactivity, associated with the metal M_1 in the figure. These react with a hydrocarbon to give water and a partially oxidized organic compound rather than CO_2 . The surface sites are reoxidized by other components of the solid catalyst rather than by O_2 directly. A second metal plays the role of an intermediary and oxygen is transported as ions through the bulk of the mixed metal oxide catalyst. A compensating transport of electrons and reaction of O_2 with the surface at sites different from those where the hydrocarbon is adsorbed make the process cyclic. Essentially this same pattern has already been illustrated by the Wacker oxidation, whereby the hydrocarbon reacts with an oxide, H_2O , in a step mediated by palladium, and a second metal, eg, copper, reacts with O_2 and then reoxidizes the palladium.

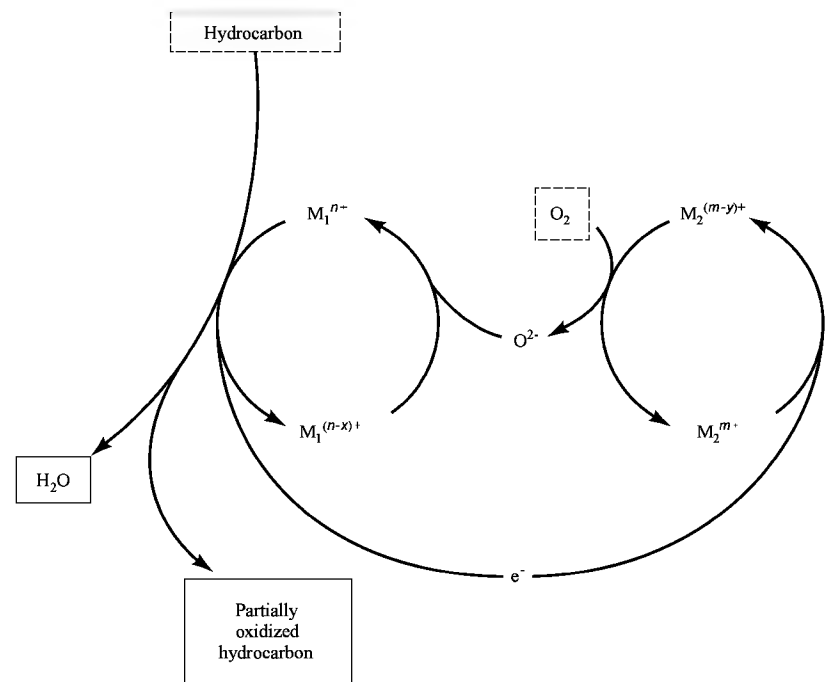
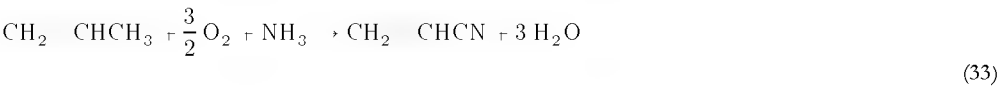


Fig. 18. Schematic representation of the catalytic cycle for ammoxidation of propylene and related reactions. M_1 and M_2 represent the two metals in a mixed metal oxides catalyst (10).

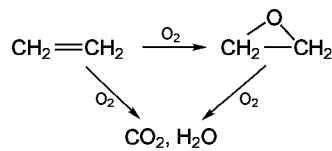
An important industrial partial oxidation process is the conversion of propylene to acrylonitrile (26):



The first catalysts used commercially to convert the propylene with high selectivity were mixed oxides of bismuth and molybdenum, referred to as bismuth molybdates. Improved catalysts consisting of a number of solid phases have been developed, with each generation becoming more complicated than its predecessor. Among the catalysts cited in a patent is the following: $\text{Co}^{2+}\text{-Ni}^{2+}_2\text{-Fe}^{3+}_3\text{Bi}^{3+}$ (MoO_4)₁₂ on 50 wt % SiO_2 with some P and K (88). Silica is the support. The other components provide new functions, perhaps making the catalyst more stable. The catalysts are mechanically stable and used in fluidized-bed reactors at low pressures $\sim 100\text{ kPa}$ ($\sim 1\text{ atm}$), and temperatures of about $400\text{--}500^\circ\text{C}$.

Catalysis by Supported Metals. Metals used in industrial catalysis are often expensive, and they are predominantly used in a highly dispersed form. Metal species dispersed on supports may be as small as the mononuclear chromium and titanium complexes used for olefin polymerization, or they may be clusters containing a small number of atoms, eg, organometallic clusters for ethylene glycol synthesis, or they may be particles with dimensions of micrometers (89). The larger particles have three-dimensional structures and resemble small chunks of metal. Their surfaces expose a number of different crystal faces, and if the particles are larger than about 5 nm the distribution of crystal faces seems to be almost independent of particle size and shape. The smaller particles (clusters), however, are less like bulk metals and are more likely to have unique structures and catalytic properties. The interactions between the metals and the support may be thought of as effects comparable to the ligand effects in molecular catalysis; the catalytic properties are sensitive to the structure and size of the metal cluster. Much remains to be learned about these materials.

Ethylene Oxidation to Ethylene Oxide. A thoroughly investigated reaction catalyzed by a supported metal is the commercially applied partial oxidation of ethylene to give ethylene oxide (90). The desired reaction is the formation of ethylene oxide, ie, epoxidation; the following reaction scheme is a good approximation:



The selective oxidation is catalyzed by silver, which is the only good catalyst. Other olefins are not converted selectively to the epoxides in the presence of silver. However, propylene epoxidation is applied commercially; the catalysts are either molybdenum complexes in solution or solid $\text{TiO}_2\text{-SiO}_2$ (see ETHYLENE OXIDE; PROPYLENE OXIDE).

The ethylene epoxidation catalysts (Fig. 9) are multicomponent mixtures consisting of a support ($\alpha\text{-Al}_2\text{O}_3$), the catalytically active component (silver particles), and chemical promoters (alkali metal ions such as Cs^+), and a binder; the older literature also describes textural promoters. Furthermore, trace amounts of chlorine-containing compounds such as ethylene dichloride are continuously added with the feed; these compounds, like the alkali metal promoter, increase the selectivity of the catalyst for ethylene oxide. The data of Figure 19 illustrate the role of an alkali metal promoter (91). Extremely small amounts of the promoter markedly improve the selectivity of the catalyst; selectivities as high as 80% are reported. Under conditions of the catalytic oxidation, the silver surface is covered with a layer of oxygen and may be more properly described as an oxide than as a metal. There is only an incomplete understanding of the nature of the catalytic sites, the role of promoters, and the bonding of the reactants to the catalyst surface.

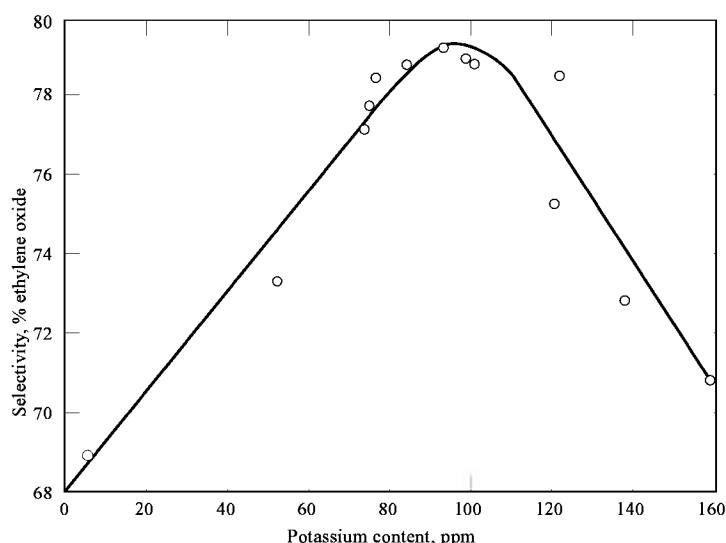


Fig. 19. Promotion of ethylene oxidation by potassium. The selectivity is the percentage of ethylene converted to ethylene oxide (91).

The support needs to be inert, which explains the choice of α - Al_2O_3 ; most metal oxides, including transition aluminas, catalyze unselective oxidation. The catalyst has a low surface area, about $1 \text{ m}^2/\text{g}$, and large pores to minimize the influence of intraparticle diffusion, which would reduce the selectivity.

Naphtha Reforming and Bifunctional Catalysis. In some supported metal catalysts the support is not just an inert platform but plays an active catalytic role. This point is illustrated by catalysts for reforming of naphtha to make high octane number gasoline, a process which is a classic example of bifunctional surface catalysis (92). The catalysts consist of metal, originally platinum (93), but now largely rhenium–platinum, on a transition alumina, γ - Al_2O_3 or η - Al_2O_3 . Platinum is chosen because it is more active than any metal except iridium in a number of reactions that increase the octane number of paraffins without substantially changing their molecular weights. These reactions include dehydrogenation, eg, conversion of methylcyclohexane to toluene, and dehydrocyclization, eg, conversion of *n*-heptane to toluene. Skeletal isomerization is also desired, but platinum has only a low activity for this reaction. Rather, the reaction is acid catalyzed. Consequently, platinum supported on an amorphous solid acid is a good catalyst.

The support must not be too strongly or too weakly acidic; chlorided Al_2O_3 is optimal. The catalyst works well for reforming although the individual functions, ie, the metal and the acid, alone do not. The metal alone does not catalyze the branching reactions; they require an acidic function to generate carbenium ions, which undergo the desired isomerization. The acidic function alone is not sufficient to generate the carbenium ions because it is too weakly acidic to protonate paraffins; if it were so strongly acidic, the catalyst would be deactivated rapidly by carbonaceous deposits. The metal in the catalyst catalyzes dehydrogenation of paraffins to give olefins, which are easily protonated and thereby converted by carbenium ion routes.

Some reforming processes operate with platinum on alumina catalysts at about 500°C and high pressures, eg, 5 MPa (50 atm), with the reactant stream containing predominantly hydrogen (26,94). It is unusual for a process in which hydrogen is produced to be carried out in the presence of excess hydrogen, but this is done to minimize catalyst deactivation. Coke causes deactivation, but the high partial pressure of hydrogen retards coke formation as aromatic coke precursors and coke are hydrogenated. Catalyst regeneration by controlled coke burnoff may be needed only about twice a year.

However, there is a disadvantage to the high hydrogen partial pressures that became especially apparent with the removal of tetraethyllead from gasoline and an increased need for reforming processes as a source of high octane number hydrocarbons. Aromatic compounds have high octane numbers, and the dehydrogenation of naphthenes, ie, cyclic paraffins, to give aromatics is favored thermodynamically at high temperatures and low hydrogen partial pressures. Therefore, there was an incentive to find a way to operate reforming processes economically at much lower pressures.

Low pressure operation became routine with the application of new catalysts that are resistant to deactivation and withstand the low pressures. The catalysts are bimetallic; most incorporate rhenium as well as platinum (95). The structures of these catalysts are still not well understood, but under some conditions the two metals form small alloylike structures, which resist deactivation better than the monometallic catalyst.

There are now a number of applications of supported bimetallic catalysts. In some instances, the role of the added metal is to isolate the atoms of the other metal at the surface, thereby reducing the rates of reactions that require ensembles of the atoms as the catalytic sites. These reactions are called structure-sensitive reactions (96). Some reactions, such as olefin hydrogenation, are structure-insensitive reactions; they seem to be catalyzed by isolated metal centers on surfaces, much as the Wilkinson hydrogenation is catalyzed by mononuclear metal complexes. Iridium–platinum catalysts have been used for naphtha reforming, and one of the roles of the platinum may be to combine with the iridium in alloylike bimetallic clusters to suppress an undesired structure-sensitive reaction, namely, paraffin hydrogenolysis (97). This reaction takes place in reforming and is largely undesired because it reduces the molecular weight range.

Catalysis by Metal Sulfides. Metal sulfides such as MoS_2 , WS_2 , and many others catalyze numerous reactions that are catalyzed by metals (98). The metal sulfides are typically several orders of magnitude less active than the metals, but they have the unique advantage of not being poisoned by sulfur compounds. They are thus good catalysts for applications with sulfur-containing feeds, including many fossil fuels.

Metal sulfide catalysts are widely applied in hydroprocessing of petroleum. The reactions include hydrogenation, hydrodesulfurization, and hydrodenitrogenation (99). Hydrodesulfurization is the reaction of organosulfur compounds with hydrogen to give hydrocarbons and H_2S ; hydrodenitrogenation gives hydrocarbons and ammonia. Hydrodesulfurization is carried out to remove sulfur from feeds to naphtha reformers because the metals in the reforming catalysts are poisoned by sulfur. Hydrodesulfurization of heavy petroleum fractions is carried out to minimize formation of SO_x resulting from combustion of the fuels. Hydrodenitrogenation is carried out to remove basic nitrogen-containing compounds from fuels that are later hydrocracked, as hydrocracking catalysts have acidic components that are poisoned by the basic nitrogen-containing compounds.

MoS_2 is one of the most active hydroprocessing catalysts, but it is expensive, and the economical way to apply it is as highly dispersed material on a support, γ - Al_2O_3 . The activity of the supported catalyst is increased by the presence of promoter ions, Co^{2+} or Ni^{2+} . The structures of the catalysts are fairly well understood; the MoS_2 is present in layers only a few atoms thick on the support surface, and the promoter ions are present at the edges of the MoS_2 layers, where the catalytic sites are located (100,101).

The catalysts are prepared by impregnating the support with aqueous salts of molybdenum and the promoter. In acidic solutions, molybdate ions are present largely in the form of heptamers, $[\text{Mo}_7\text{O}_{24}]^{4-}$, and the resulting surface species are believed to be present in islands, perhaps containing only seven Mo ions (100). Before use, the catalyst is treated with H_2 and some sulfur-containing compounds, and the surface oxides are converted into the sulfides that are the catalytically active species.

The applications of supported metal sulfides are unique with respect to catalyst deactivation phenomena. The catalysts used for processing of petroleum residua accumulate massive amounts of deposits consisting of sulfides formed from the organometallic constituents of the oil, principally nickel and vanadium (102). These, with coke, cover the catalyst surface and plug the pores. The catalysts are unusual in that they can function with masses of these deposits that are sometimes even more than the mass of the original fresh catalyst. Mass transport is important, as the deposits are typically formed

with effectiveness factors less than unity, and in the extreme case the deposits block the pore mouths. Modeling of the transport reaction phenomena has guided the preparation of catalysts with tailored pore structures to minimize the detriment of the deposits (103). These have been some of the most fruitful applications of the principles of chemical engineering in catalyst design and preparation.

Catalyst Development, Testing, and Production

Catalysts are discovered to meet processing needs and opportunities, but the discovery of a catalytic application to take advantage of some newly discovered material almost never occurs. Catalyst development is largely a matter of trial and error testing. The methodology was defined by Haber, Bosch, and Mittasch in the development of the ammonia synthesis process. Catalyst developers benefit from an extensive and diverse literature and often can formulate good starting points in a search for candidate catalysts by learning what has been used successfully for similar reactions. Deeper insights, such as would arise from understanding of the mechanistic details of a catalytic cycle, are usually not attainable; the exceptions to this rule largely pertain to molecular catalysis, usually reactions occurring in solution. Fundamental insights were valuable in guiding the development of the process for chiral hydrogenation and that for methanol carbonylation, among others, but it would be inappropriate to infer that understanding of the fundamental chemistry led to straightforward design of the catalysts. Indeed, the initial working hypothesis about the chiral hydrogenation turned out to be incorrect. The more complicated processes of surface catalysis are for the most part only partially understood even when the processes are established and extensive after-the-fact research has been done. Creative research in catalyst discovery and development is usually the result of intuition and partial understanding combined with efficient testing and serendipity. Researchers who are repeatedly successful in finding new and improved catalysts seem to recognize needs and opportunities and notice significant exceptions to expected patterns and reason inductively by imperfect analogies.

Catalyst testing and evaluation have been revolutionized by computers, automated test reactors, and analytical methods. With modern equipment, researchers can systematically prepare and screen many catalysts in a short time and efficiently determine, not only the initial catalytic activity and selectivity, but also the stability and the appearance of trace products that may indicate some new catalytic properties worthy of further development.

Catalyst design is in a primitive stage. There are hardly any examples of true design of catalysts (42). However, development of improved catalysts has been guided successfully in instances when the central issues were the interplay of mass transport and reaction. An example is catalysts used for hydroprocessing of heavy fossil fuels.

Almost all industrial catalysts are developed by researchers who are motivated to improve processes or create new ones. Thus the organization that first uses a new catalyst is usually the one that has discovered it. This organization, however, only rarely becomes the manufacturer of the catalyst used on a large scale. Catalysts are for the most part highly complex specialty chemicals, and catalyst manufacturers tend to be more efficient than others in producing them. Catalyst manufacturing is a competitive industry. Catalyst users often develop close relations with catalyst manufacturers, and the two may work together to develop and improve proprietary catalysts.

The Catalysis Literature

Catalysis is a broad, complex subject that is documented in many and varied sources. The field is rich in opportunity, in part because there is so much information that it is possible to find nuggets that competitors miss. Industrial catalysis is a competitive field, and much practical knowledge is proprietary.

The literature consists of patents, books, journals, and trade literature. The examples in patents may be especially valuable. The primary literature provides much catalyst performance data, but there is a lack of quantitative results characterizing the performance of industrial catalysts under industrially realistic conditions. Characterizations of industrial catalysts are often restricted to physical characterizations and perhaps activity measurements with pure component feeds, but it is extremely rare to find data characterizing long-term catalyst performance with impure, multicomponent industrial feedstocks. Catalyst regeneration procedures are scarcely reported. Those who have proprietary technology are normally reluctant to make it known. Readers should be critical in assessing published work that claims a relevance to technology.

Often the catalysts described in the literature are not quite the same as those used in industrial processes, and often the reported performance is for pure single-component feeds. Sometimes the best quantitative approximations that can be made from the available literature are those based on reported kinetics of reactions with pure feeds and catalysts that are similar to but not the same as those used in practice. As a first approximation, one may use the published results and scale the activity on the basis of a few laboratory results obtained with realistic feeds and commercially available catalysts.

Catalyst suppliers are valuable sources of information. They often have extensive experience testing catalysts in long-term operation with real industrial feedstocks and may be willing to share information to improve their chances of selling a catalyst. Also they may work with a potential customer to develop catalysts that they could then supply. There is an extensive literature produced by catalyst manufacturers and organizations that license and market catalytic technology. This trade literature should be read critically as its purpose is to generate sales, but it often contains valuable information. Catalyst manufacturers and those who license and sell technology are motivated to demonstrate their technical knowledge. Their success in marketing depends on their technical reputations and their reliability in supplying catalysts and technology that consistently meet specifications.

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CATALYSIS, PHASE-TRANSFER

Phase-transfer catalysis (PTC) is a technique by which reactions between substances located in different phases are brought about or accelerated. Typically, one or more of the reactants are organic liquids or solids dissolved in a nonpolar organic solvent and the coreactants are salts or alkali metal hydroxides in aqueous solution. Without a catalyst such reactions are often slow or do not occur at all; the phase-transfer catalyst, however, makes such conversions fast and efficient. Catalysts used most extensively are quaternary ammonium or phosphonium salts, and crown ethers and cryptates. Although isolated examples of PTC can be found in the early literature, it is only since the middle of the 1960s that the method has developed extensively.

Traditionally, the reactions to be considered here are performed in homogenous medium, either in hydroxylic solvents or in polar aprotic solvents. In comparison, PTC has the following advantages: no need for expensive aprotic solvents; simpler work-up; shorter reaction time and or lower reaction temperature; use of aqueous alkali hydroxides instead of other expensive bases.

Undoubtedly cost factors and environmental considerations (recycling of solvents, less toxic or less hazardous materials) will lead to increasing industrial application of this methodology.

The Fundamental Process in Displacement Reactions

Figure 1 shows the mechanistic picture developed by C. M. Starks (1,2) for liquid–liquid PTC in a graphical form. The catalyst cation Q^+ extracts the more lipophilic anion Y^- from the aqueous to the nonpolar organic phase where it is present in the form of a poorly solvated ion pair $[Q^+ Y^-]$. This then reacts rapidly with RX , and the newly formed ion pair $[Q^+ X^-]$ returns to the aqueous phase for another exchange process: $X^- \rightarrow Y^-$. In practice most catalyst cations used are rather lipophilic and do not extract strongly into the aqueous phase so that the anions are exchanged at the phase boundary.

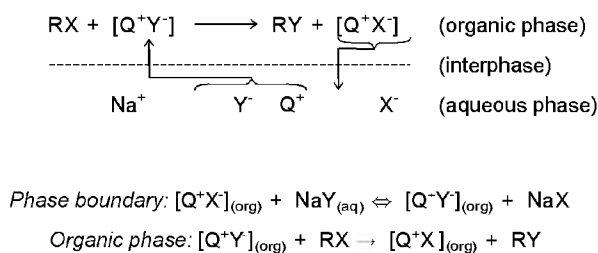


Fig. 1. Mechanism for liquid–liquid PTC.

This general scheme has been supported by a wealth of detailed investigations. The organic-phase reaction is usually rate limiting. Of special importance are the observations that the rate of reaction is proportional to the catalyst concentration and independent of the stirring speed (size of the interphase) above the minimum required for efficient mixing. A certain number of water molecules are coextracted with the anion (3). This phenomenon has a decisive influence on the relative, eg, Cl vs Br vs I, and absolute rate of reaction. In solvents of relative low polarity, eg, CH_2Cl_2 , $CHCl_3$, benzene, the ion pair, not the anion, is the dominant nucleophile (4). Absolute rates may be higher than in polar aprotic solvents.

Types of Phase-Transfer Processes

There are several types of processes depending on the nature of the phases, the character of the extracted species, and the direction of extraction.

Phases. Often there are two liquid phases (liquid–liquid PTC) or one solid, one liquid (solid–liquid PTC). If the catalyst is bound to a polymeric matrix this may comprise a third phase (triphasic catalysis). Examples of gas–liquid, gas–solid, and solid–solid PTC are still relatively rare. In the latter two cases, a small amount of liquid, eg, water, is probably present as an unnoticed third phase.

Character of the Extracted Species. Most PTC reactions are initiated by the extraction of some anion, be it a nucleophile, a base, or an oxidant, by lipophilic cations. However, relatively hydrophilic cations can be extracted by large anions from an aqueous or solid phase into an organic solvent for electrophilic reactions. These include, for instance, diazonium ions and stable carbocations. But applications of this type are not yet widespread. Uncharged compounds HY can also be transferred if they form relatively strong hydrogen bonds to the halide in NR_4X catalysts. Among these are hydrogen halides, phenols, carboxylic acids, hydrogen peroxide, hydrazine, and even amines. Complexes, eg, $[NR_4^+ Cl^- \cdots HCl]$, are known in crystalline form. A last group of extracted species are metal atoms. Crown ethers can make alkali metals soluble in solvents like THF for reductions; anthracene solubilizes magnesium.

Direction of Extraction. The "normal" PT process involves the transfer of a reactive agent from a solid or aqueous environment into a nonpolar organic solvent. But the exact opposite can be executed: extraction from an organic phase into an aqueous phase, for example, for changing selectivities. This "inverse PTC" is done relatively rarely.

Types of Phase-Transfer Reactions

There is an enormous potential of PTC for numerous reactions and no single type of mechanism explains everything. Among the more frequently used reactions involving anion extraction, two classes can be distinguished: (1) reactions without added bases; and (2) reactions in the presence of alkali metal hydroxides, potassium carbonate, or other inorganic bases. Numerous substitutions $RX + Y^- \rightarrow RY + X^-$ are of the first type. The leaving group, X^- , is normally a halide or sulfonate, and the nucleophile can be almost any anion, eg, halide, CN^- , SCN^- , N_3^- , NO_2^- , carboxylate, phenolate, sulfide, thiolate, and many others. Another group of reactions without added base are oxidations with permanganate, hypochlorite, chlorite, chlorate, peroxydisulfate, $[Ce(NO_3)_6]^{2-}$, hexacyanoferrate(III), superoxide radical-anion, hydrogen peroxide, perborate, and others. Reductions with complex hydrides, dissolving metals, dithionite, formate, and others, as well as transfer hydrogenations can also be accelerated by phase-transfer catalysts.

Class (2) reactions are performed in the presence of dilute to concentrated aqueous sodium hydroxide, powdered potassium hydroxide, or, at elevated temperatures, solid potassium carbonate, depending on the acidity of the substrate. Alkylations are possible in the presence of concentrated NaOH and a PT catalyst for substrates with conventional pK_a values up to ~ 23 . This includes many C–H acidic compounds such as fluorene, phenylacetylene, simple ketones, phenylacetonitrile. Furthermore, alkylations of N–H, O–H, S–H, and P–H bonds, and ambident anions are well known. Other basic phase-transfer reactions are hydrolyses, saponifications, isomerizations, H/D exchange, Michael-type additions, aldol, Darzens, and similar

additions to multiple hetero bonds, β -eliminations, and basic autoxidations. Additional reactions of this class are α -eliminations to form carbenes, Wittig- and Horner-Emmons reactions, reactions of sulfonium ylides, a multitude of rearrangements, etc.

There are two very active special fields of phase-transfer applications that transcend classes (1) and (2): metal–organic reactions both with and without added bases, and polymer chemistry. Certain chemical modifications of side groups, polycondensations, and radical polymerizations can be influenced favorably by PTC.

Factors Influencing the Usefulness of Phase-Transfer Catalysis

In the following reaction under phase catalytic conditions



the relative rate for $X = \text{Cl}, \text{Br}, \text{I}$ is determined by two factors: the actual chemical reaction with $\text{I}, \text{Br},$ or Cl ; and the magnitude of the competitive extraction of Y^- vs X^- . If the second factor is very unfavorable for Y^- , PTC may be impossible. Thus it is important to have some insight into the order of magnitude of the factors involved. The conditional extraction constant E_{QX} of the salt QX is defined as:

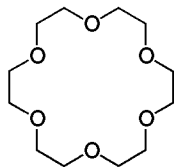
$$E_{\text{QX}} = \frac{[\text{QX}]_{(\text{org})}}{[\text{Q}^+]_{(\text{aq})} \cdot [\text{X}^-]_{(\text{aq})}}$$

where the bracketed expressions stand for activities, or concentrations, in organic or aqueous media, respectively.

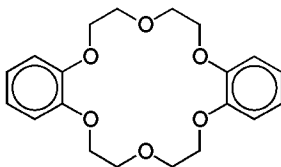
Solvent. For PTC the solvents should be nonmiscible with water and non-hydroxylic; CHCl_3 and CH_2Cl_2 , chlorobenzene, toluene, acetonitrile, and even petroleum ethers are employed. Alternatively, one can work without extra solvent if the substrate is liquid.

Catalyst Cation. The logarithms of extraction constants for symmetrical tetra-*n*-alkylammonium salts ($\log E_{\text{QX}}$) rise by ca 0.54 per added C atom. Although absolute numerical values for extraction coefficients are vastly different in various solvents and for various anions, this relation holds as a first approximation for most solvent–water combinations tested and for many anions. It is important to note, however, that the lipophilicity of phenyl and benzyl groups carrying ammonium salts is much lower than the number of C atoms might suggest. Benzyl is extracted between *n*-propyl and *n*-butyl. The extraction constants of tetra-*n*-butylammonium salts are about 140 times larger than the constants for tetra-*n*-propylammonium salts of the same anion in the same solvent–water system.

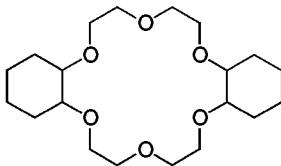
For practical application in mixtures of water–organic solvent, only ammonium and phosphonium salts containing 15 or more C atoms are sufficiently lipophilic. In empirical catalyst comparisons crown ethers (hexaoxacyclooctodecanes) (1)–(3) were often as effective as the best onium salts.



(1)



(2)



(3)

Other complexing agents sometimes advocated are cryptates, especially the compound dubbed [2.2.2] (Kryptofix 222) [23978-09-8] (see CHELATING AGENTS). Crown ethers were originally advocated for reactions in the presence of solid reagents (liquid–solid PTC). It is now known, however, that onium salts are equally suitable in many cases.

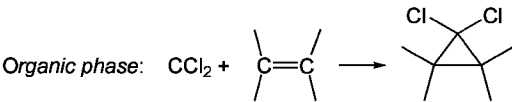
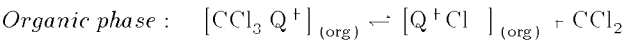
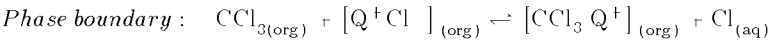
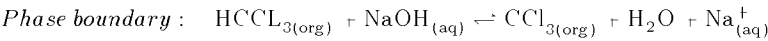
Often poly(ethylene glycol)s or derivatives thereof can be used instead of crowns or onium salts advantageously, although their catalytic activity frequently tends to be somewhat lower. The possible toxicity of crowns and cryptands and the price difference between these compounds and onium salts (100:1 to 10:1) are other important factors to be considered. Thus (1) [17455-13-9], (2) [14187-32-7], and (3) [16069-36-6] and cryptands are used more often in laboratory work, whereas onium salts are more important for industrial processes.

Benzyltriethylammonium chloride [56-37-1] is the most widely used catalyst under strongly basic conditions. Methyltriocetylammmonium chloride [5137-55-3] (Aliquat 336, Adogen 464) is probably the least expensive catalyst. Others of high activity and moderate price are tetra-*n*-butylammonium chloride [1112-67-0], bromide [1643-19-2], hydrogen sulfate [32503-27-8], tetra-*n*-butylphosphonium chloride [2304-30-5], and other phosphonium salts of a similar number of C atoms. Many other onium salts can also be utilized.

Stability. The stability of the catalysts is another important factor. Reactive nucleophilic anions can attack their own counter ion, leading to Hofmann-type elimination or simple dequaternization. Rates of these processes can vary from zero to very fast depending on structures both of anion and cation, solvent, temperature, and especially the presence and concentration of alkali metal hydroxides. Contrary to an earlier suggestion, quaternary phosphonium salts are generally not more stable than ammonium salts. High temperature stabilities (up to ca 200°C) are exhibited by 4-dialkylaminopyridinium salts such as (4) [93103-34-5] (5), tetraphenylarsonium chloride (5) [507-28-8] (6), and especially the phosphoiminium salts bis[tris(dimethylamino)phosphine]iminium chloride [123048-82-8] (6) and tetrakis[tris(dimethylamino)phosphine]iminium chloride [122951-89-7] (7). Only the last two catalysts are also very stable in the presence of hot concentrated NaOH (6).

phase. Catalyst action is seen in detaching substrate anions from the boundary by anion exchange. The competitive situation for this is very favorable since most organic weak acids are much more lipophilic than halide ions except for iodide. Supporting evidence for the importance of interfacial processes is that some closely related alkylations proceed without catalyst in systems with negligible mutual solubility of the phases.

In dihalocarbene generation by phase-transfer catalysis the following steps seem to be involved (15): formation of CX_3^- anions dynamically anchored at the boundary; reversible detachment with the help of the catalyst; reversible carbene formation $[Q^+CX_3] \rightleftharpoons [Q^+X] + CX_2$; addition to olefin.



In practice, 1–10 mol % of catalyst are used most of the time. Regeneration of the catalyst is often possible if deemed necessary. Some authors have advocated systems in which the catalyst is bound to a polymer matrix (triphase-catalysis). Here separation and generation of the catalyst is easy, but swelling, mixing, and diffusion problems are not always easy to solve. Furthermore, triphase-catalyst decomposition is a serious problem unless the active groups are crowns or poly(ethylene glycol)s. Commercial anion exchange resins are not useful as PT catalysts in many cases.

Typical Applications

From the many thousands of patents and journal publications, only a few typical examples are given here.

Displacement Reactions. The reactions $RCI \rightarrow RCN$ are carried out by heating a threefold excess of concentrated aqueous NaCN solution with the alkyl chloride and 2 mol % tributylhexadecylphosphonium bromide for 2 h (1) (see NITRILES).

Formation of Esters. $RBr \rightarrow RCOOCH_3$ proceeds in 1–2 h by heating a concentrated CH_3COOK solution with the halide, with or without solvent, and 1 mol % Aliquat 336 catalyst at 100°C (16). Esterification of higher acids, including sterically hindered ones, is carried out by neutralizing one equivalent of acid and one equivalent of tetrabutylammonium hydrogen sulfate with two moles of aqueous sodium hydroxide and boiling the mixture with the alkylating agent in CH_2Cl_2 for 15–30 min (17) (see ESTERIFICATION).

Formation of Ethers. Very high ether yields can be obtained from alcohols and phenols with dialkyl sulfates in CH_2Cl_2 and concentrated NaOH–tetrabutylammonium chloride at room temperature or slightly elevated temperature within 1–5 h (18). Using excess aqueous caustic– $N(C_4H_9)_4HSO_4$, unsymmetrical aliphatic ethers can be prepared with alkyl chlorides at 25–70°C in 3–4 h (19) (see ETHERS).

Alkylation of Carbanions. Concentrated NaOH–benzyltriethylammonium chloride is the base–catalyst system normally used for this type of process (20). Classes of compounds alkylated in this way include: phenylacetoneitriles, benzylketones, simple aliphatic ketones, certain aldehydes, aryl sulfones, β-ketosulfones, β-ketoesters, malonic esters and nitriles, phenylacetic esters, indene, and fluorene (see ALKYLATION).

Nucleophilic Aromatic Substitution. An activated aromatic halide is heated at 100–200°C with the alkali metal salt of the nucleophile (ArO^- , RO^- , F^- , CN^- , Cu^+ , carbanion, etc) and the catalyst in an inert solvent (toluene, chlorobenzene) for a few minutes to a day (21–24).

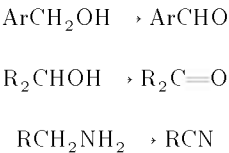
Alkylation of N-Heterocycles. Indoles (25), imidazoles (26), pyrazoles (27), benzotriazoles (27), or other heterocycles are generally alkylated in the presence of 50% aqueous NaOH and catalyst benzyltriethylammonium chloride without solvent or in chlorobenzene or toluene.

Polymerization of Butyl Acrylate. An aqueous solution of $K_2S_2O_8$ and a solution of butyl acrylate [141-32-2] and catalytic amounts of Aliquat 336 in ethyl acetate are heated at 55°C (28) (see ACRYLIC ESTER POLYMERS).

Oxidations.

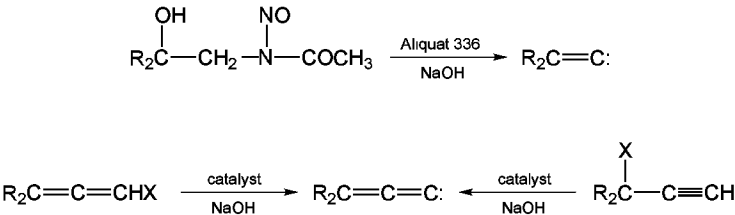
KMnO₄. In neutral solution with Aliquat 336 and benzene as organic solvent, olefins yield carboxylic acids (1,29).

NaOCl. Sodium hypochlorite proves to be a useful reagent under PTC conditions for the following transformations (30):



Applications of phase-transfer catalysis with these additional oxidants are known: peracetic acid, air–KOH, $K_3[Fe(CN)_6]$, KO_2 , K_2CrO_4 , H_2O_2 –heavy-metal oxide (31), H_5IO_6 , ceric ammonium nitrate, KNO_2 , $NaBrO_3$, and $NaClO_2$.

Carbene Reactions. The best procedure for preparing dihalocarbene adducts of olefins consists in stirring a haloform–methylene chloride solution with an excess of concentrated aqueous caustic soda in the presence of benzyltriethylammonium chloride. Even sterically hindered and electronically deactivated compounds give excellent yields (32). Mixed dihalocarbenes, CXY ($X, Y = F, Cl, Br, I$), except for CF_2 , can be prepared. Insertions into tertiary C–H bonds can be carried out with moderate yields. Among other less common reactions improved by the use of PTC-generated CCl_2 are the carbylamine synthesis ($RNH_2 \rightarrow R-NC$) (33). Alkylidene carbene ($R_2C=C:$) and alkenylidene carbene ($R_2C=C=C:$) adducts have also been prepared (34,35).



Other reactions assisted by PTC are described in the general references.

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CATALYSTS

Supported,
Regeneration,

SUPPORTED

Supported catalysts comprise the largest group of materials capable of catalysis, which is broadly defined as the acceleration of chemical reactions (see CATALYSIS). Supported catalysts are extremely useful in virtually all areas of petroleum refining and chemical processing, which accounts for the fact that as a group they were the principal contributor to the \$2.5 billion–\$3.0 billion worldwide catalyst industry in 1990. Petroleum refining catalysts comprised 37% of the \$1.8 billion U.S. market in 1990, whereas chemical processing made up an additional 34% and emission control catalysts contributed 29% (1). Of the \$1.0 billion petroleum refining catalyst market, 56% of revenues came from fluid cracking catalysts (FCC), 31.5% from hydrotreating catalysts, 6.5% from hydrocracking catalysts, and 4.5% from reforming catalysts (2).

An annual review of the worldwide catalyst industry identifies current technical and business trends within the catalyst industry and lists virtually all industrial supported (and other) catalysts by manufacturers' designations (3). Included are the applications for the catalysts, the composition, ie, active agents and support materials, and some physical properties.

Although it is impossible to cover every supported catalyst herein, examples that illustrate the general principles of catalysis have been chosen. Also, the reader is encouraged to consult the literature references, especially texts and reviews (4–6). Some novel approaches to using supported catalysts have evolved in the past several years, among which are inorganic membrane reactors, the automotive catalytic converter and catalytic distillation technology, which is used in the manufacture of methyl *t*-butyl ether and certain aromatics using catalysts such as zeolites contained in fiber glass cloth stainless steel mesh bales packed in what is essentially a distillation column (7).

Definition of Supported Catalysts

Supported catalysts are solid or heterogeneous catalysts in which relatively small amounts of catalytically active species, frequently metals, are deposited on the surface of largely inert, porous, shaped support bodies, such as pellets, rings, extrudate, and granules, which are sometimes referred to as carriers. Most materials used in catalyst supports are comprised of single- or mixed-metal oxides, such as alumina, silica, magnesia, titania, zirconia, and aluminosilicates. This definition is sufficient to describe supported catalysts as they are used in industrial applications, but it does not recognize the fact that virtually all solid catalysts may be viewed as supported catalysts because in all solids, with the exception of very small clusters, the atoms in the surface, especially at the edges and corners of crystals or crystallites, are demonstrably different from those in the bulk. Surface atoms must invariably have a lower coordination number, ie, a smaller number of nearest neighbor atoms. The number of absent nearest neighbors of a surface atom compared with an atom of the same element in the bulk solid defines the surface atom's capacity for vacancies. A vacancy on a surface atom is one of the better ways to visualize a catalytic site, since it is a location into which a reactant molecule may donate electron density, which is the first step in the process of activating that molecule in the catalyzed reaction (5).

Advantages of Supported Catalysts

Separability. One of the greatest advantages of a solid catalyst is that it can be separated easily from the products of reaction. To do this successfully requires careful control of the process conditions so that exposure of the catalyst to nonreactant liquids capable of affecting or dissolving either the catalytic material or the support is prevented or minimized. Solid catalysts typically are used in axial or radial flow beds and multitubular reactors. Many successful commercial processes maintain the reactants and products in the gas phase while in contact with the catalyst to avoid catalyst degradation problems.

In some liquid-phase processes, catalyst components are slowly leached from the catalyst bed and eventually the catalyst must be replaced. The feasibility of this type of process involves economics, ie, the costs of catalyst maintenance and keeping a unit out of service for catalyst replacement, and product quality and safety, ie, the effects of having catalyst components in the product and their ease of removal.

Cost. The catalytically active component(s) in many supported catalysts are expensive metals. By using a catalyst in which the active component is but a very small fraction of the weight of the total catalyst, lower costs can be achieved. As an example, hydrogenation of an aromatic nucleus requires the use of rhenium, rhodium, or ruthenium. This can be accomplished with as little as 0.5 wt % of the metal finely dispersed on alumina or activated carbon. Furthermore, it is almost always easier to recover the metal from a spent supported catalyst bed than to attempt to separate a finely divided metal from a liquid product stream. If recovery is efficient, the actual cost of the catalyst is the time value of the cost of the metal less processing expenses, assuming a nondeclining market value for the metal. Precious metals used in catalytic processes are often leased.

Catalyst Activity. Of utmost importance in the design of most catalysts is activity, which is a measure of the ability of a catalyst to effect conversion of the reactant(s) to the desired product(s) under specified conditions. In industrial applications, catalyst activity is usually discussed in terms of the percent conversion of a reactant under given conditions of temperature, pressure, and contact time.

Since catalyst activity is dependent on how much catalytically active surface is available, it is usually desirable to maximize both the total surface area of the catalyst and the active fraction of the catalytic material. It is often easier to enlarge the total surface area of the catalyst than to increase the active component's surface area. With proper catalyst design, however, it is possible to obtain a much larger total active surface area for a given amount of metal or other active material in a supported catalyst than can be achieved in the absence of a support.

In service, supported catalysts frequently undergo loss of activity over a period of time. In many cases, such catalyst deactivation is accompanied by the loss of accessible surface area of the active phase by sintering, by the accumulation of poisons, or by conversion of active sites to inactive species.

Catalyst Selectivity. Selectivity is the property of a catalyst that determines what fraction of a reactant will be converted to a particular product under specified conditions. A catalyst designer must find ways to obtain optimum selectivity from any particular catalyst. For example, in the oxidation of ethylene to ethylene oxide over metallic silver supported on alumina, ethylene is converted both to ethylene oxide and to carbon dioxide and water. In addition, some of the ethylene oxide formed is lost to complete oxidation to carbon dioxide and water. The selectivity to ethylene oxide in this example is defined as the molar fraction of the ethylene converted to ethylene oxide as opposed to carbon dioxide.

In order to optimize selectivity for any particular system, unwanted by-products must be identified, and reaction conditions and catalyst components that are not favorable to their formation selected. For many reactions, selectivity is found to decrease as the activity increases. Thus sometimes it is necessary to accept a compromise in which some activity or selectivity or both is sacrificed so that the overall product yield or process economics is maximized.

Support Materials

The objective in selecting a support for a catalytic application is to provide a suitable, stable base for the active catalytic component. The support should be chemically inert so that it does not interfere with the role of the catalytic component, and it should possess acceptable physical properties for the intended application. The support should retain its dimensions and chemical integrity under the conditions necessary to operate the catalytic process.

Composition. Among the most commonly used support materials are aluminas, silicas, and aluminosilicates with a wide range of alumina to silica ratios, as well as activated carbon, silicon carbide, selected clays, various ceramics, artificial and natural zeolites, kieselguhr, and pumice. Polymeric

materials are also used as supports (see CATALYSIS; ENZYMES; ION EXCHANGE RESINS) (8). Other recognized support materials include calcium carbonate, barium carbonate and sulfate, and magnesium halides. Aluminas, silicas, and aluminosilicates are produced in large tonnage for catalyst manufacture and are available in a wide variety of chemical and physical modifications and purities. The various forms of alumina and silica derive their characteristics from the conditions used during precipitation of hydrated aluminum hydroxide and silicic acid, respectively, and the severity of calcination used to produce the final state of hydration (9,10). As chemically bound water is removed from the dried precipitates by the use of increasingly severe calcination conditions, the resulting powders become progressively less reactive and their surface areas are lowered dramatically. Alumina powders, for example, may be obtained with surface areas ranging from less than 0.2 m² g to greater than 200 m² g (see ALUMINUM COMPOUNDS, ALUMINA).

The method of preparation of a support material has a tremendous effect on its properties (11). For example, zeolites, which are highly structured aluminosilicates, are known to be extremely sensitive to the conditions employed both during and after crystallization (12). Also, when silica–titania is precipitated by a coprecipitation method using ammonia, in which localized hydroxide ion gradients are established by the precipitation process itself, the product is much more acidic than when it is precipitated using urea, which supplies hydroxide ion slowly and uniformly during precipitation (13).

Size and Shape. Although there are exceptions, catalyst support materials generally are not used in catalysts as fine powders because of the difficulty of handling and using catalysts in this form. Instead, it is common practice to form catalyst support materials into convenient sizes and shapes that satisfy the chemical and engineering needs of the overall catalytic process. Catalyst support materials in carefully controlled powder sizes are typically mixed with small amounts of temporary binders, extrusion aids, and a suitable liquid (frequently water) and are extruded or otherwise shaped into bodies with diameters as small as 0.5 mm or as large as 150 mm. Extrudates can be fabricated into an almost unlimited variety of cross-sectional shapes and cut to virtually any desired length, which varies with the application. Some of the more useful shapes are cylinders, rings, and multilobed bodies. Optionally, support materials may be tableted or pelletized to form cylindrical bodies that can be used as is or rolled into spheres. Spheres can also be produced by spray-drying and precipitation techniques. For example, spherical silica gel is a precipitated product. Techniques are available that allow the production of hollow bodies as well as bodies with a dense core and a porous outer layer.

A catalyst manufactured using a shaped support assumes the same general size and shape of the support, and this is an important consideration in the process design, since these properties determine packing density and the pressure drop across the reactor. Depending on the nature of the main reaction and any side reactions, the contact time of the reactants and products with the catalyst must be optimized for maximum overall efficiency. Since this is frequently accomplished by altering flow rates, described in terms of space velocity, the size and shape of the catalyst must be selected carefully to allow operation within the capabilities of the hardware.

Surface Area. This property is of paramount importance to catalyst performance because in general catalyst activity increases as the surface area of the catalyst increases. However because some reaction rates are strongly dependent on the nature of the structure of the catalytic surface, a linear correlation of catalyst activity with surface area should not be expected. As the catalyst surface area increases, for many reactions the selectivity of the catalyst is found to decrease. If the support material is completely inert to the reactants and products, this effect may be diminished somewhat.

The primary determinant of catalyst surface area is the support surface area, except in the case of certain catalysts where extremely fine dispersions of active material are obtained. As a rule, catalysts intended for catalytic conversions utilizing hydrogen, eg, hydrogenation, hydrodesulfurization, and hydrodenitrogenation, can utilize high surface area supports, whereas those intended for selective oxidation, eg, olefin epoxidation, require low surface area supports to avoid troublesome side reactions.

Support surface area can be varied within a wide range of values by a variety of techniques. Alumina, silica, and other metal oxide-containing support materials respond well to calcination conditions, where higher temperatures and longer calcination times can be used to obtain progressively lower surface areas in the base oxide powders. Additional control of surface area in shaped bodies can be obtained by grinding the calcined oxides to specific particle sizes, combining the powder with binders and combustible burnout materials, such as powdered cellulose, wood flour, and polymer powders, prior to shaping and recalcination. Careful control of the particle size of the burnout material powder employed can be used to induce very specific porosities and pore size distributions in the support, which, along with recalcination conditions, can define the surface area of the finished support body.

Some catalyst supports rely on a relatively low surface area structural member coated with a layer of a higher surface area support material. The automotive catalytic converter monolith support is an example of this technology. In this application, a central core of multichanneled, low surface area, extruded ceramic about 10 cm in diameter is coated with high surface area partially hydrated alumina onto which are deposited small amounts of precious metals as the active catalytic species.

In another example, TiO₂ can be deposited on a silica support body in order to obtain a stable high surface titania. This is necessary because TiO₂ sinters badly on heating in the bulk oxide and loses surface area. The TiO₂–SiO₂ combination is useful as a catalyst for the oxidation of *o*-xylene to phthalic anhydride.

Catalyst support surface area frequently is measured by one of several gas adsorption techniques, the best known of which is the BET method, which relies on the use of nitrogen or krypton adsorption isotherms at low temperatures (14). Different degrees of precision are available using single-point, triple-point, and multipoint variations of the method (15). Fast and accurate differential flowing gas adsorption methods utilizing nitrogen and helium are also available for materials with surface areas within an appropriate range. Surface areas may also be determined by mercury porosimetry.

Porosity and Pore Size. The support porosity is the volume of the support occupied by void space and usually is described in units of cm³ g. This value represents the maximum amount of liquid that may be absorbed into the pore structure, which is an especially important consideration for deposition of metal salts or other active materials on the support surface by liquid impregnation techniques. The concentration of active material to be used in the impregnating solution is determined by the support porosity and the desired level of active material loading on the catalyst. If the porosity is too low, inefficient use of the support material and reactor volume may result. If the porosity is too high, the support body may not contain sufficient solid material to provide the strength necessary to survive catalyst manufacture and handling.

The pore-size distribution and the nature of the pores in catalyst supports and hence the catalysts derived from them are important properties that significantly affect catalyst performance (16). In most cases, catalyst designers prefer an open-pore structure, that is, pores that have more than one opening, and a pore size as uniform as possible in order to obtain maximum utilization of the available pore volume. This can be achieved by careful choice of raw materials and processing conditions.

In some cases, it is desirable to have a bimodal or multimodal pore structure in which there are present both large diameter channels and smaller, intersecting passages. The larger channels facilitate penetration of impregnation solutions into the support during catalyst manufacture and also allow reactants and products to enter and leave the catalyst with minimum restrictions during operation. The smaller passageway pores contain most of the support's surface area and thus make more efficient use of the available catalyst volume than do the large channels. Zeolite-based catalysts are good examples of this type of arrangement. In most cases the zeolite selected for a particular reaction contains channels with molecular dimensions sized specifically to restrict the reactants that may enter and the products that may leave as an excellent means to enhance selectivity to a desired product.

Porosity and pore-size distribution usually are measured by mercury porosimetry, which also can provide a good estimate of the surface area (17). In this technique, the sample is placed under vacuum and mercury is forced into the pore structure by the application of external pressure. By recording the extent of mercury intrusion as a function of the pressure applied, it is possible to calculate the total pore volume and obtain the population of the various pore sizes in the range 2 nm to 10⁵ nm.

Attrition Loss. The tendency of a support body to be reduced to powder is termed susceptibility to attrition, and the measurement of such susceptibility is termed attrition loss. Attrition can occur when support bodies rub against one another and abrade the surface, such as during calcination in a rotary kiln or sizing on moving screens.

Density. This property is of secondary importance to catalyst designers but is of great relevance to manufacturers and users. Density must be taken into account when a catalyst bed is being engineered in order to assure sufficient strength in the process equipment for safe operation. In addition, the density of a catalyst support affects cost, because a higher density support requires the manufacturer to purchase greater quantities of raw materials. Since catalysts are frequently sold by weight and loaded into reactors by volume, catalyst density is always a specification required by the purchaser. Most manufacturers use support or catalyst bulk density as a measure of product uniformity in quality assurance procedures.

Cost and Quality. Many factors affect catalyst support cost including which raw materials are used, the purity of the raw materials, the chemical processing steps required, the fabrication method used, the severity of calcination conditions, and the extent of the quality assurance procedure. In

some cases, catalyst support manufacturers are able to utilize by-products of other in-house operations as raw materials for catalyst supports, which sometimes provides economies not available to other manufacturers and may also offer unique opportunities with regard to composition, chemical structure, or purity.

Design and Development of Supported Catalysts

Much progress has been made in understanding how to create and use catalysts, but the design and preparation of practical catalysts still relies on a substantial amount of art; that is, the application of known facts and intuition to trial and error methods. General principles are described in a number of texts (18–21). Very few completely new catalyst systems have been designed from first principles or completely theoretical considerations. New catalysts are much more likely to be discovered as a result of an adventitious observation than designed by intent.

Successful catalyst design requires that the very first decisions made be at least partly correct. In a typical design experiment, an element known to be catalytically active toward a certain type of reaction must be correctly combined with a support material considered to be suitable because of its chemical and physical properties. The product catalyst must be evaluated under conditions considered feasible for the reaction. If the experiment is successful, that is, if the catalyst produces conversion of the reactant and adequate selectivity to the desired product, then the experimental catalyst may be a candidate for further development. If there is inadequate activity, an attempt to obtain greater catalyst surface area may be made, or a different catalytically active element may be tried. If selectivity is poor, the catalyst support or the reaction conditions may be changed. Once a promising combination has been found, the process of developing the catalyst becomes reiterative, and a large number of variables must be optimized. Statistical methods can be of great value in optimization, but they are not particularly useful in the design or discovery phase. Today, much catalyst research is centered on improving or modifying existing catalysts.

In addition to developing satisfactory catalysts, the designer also may have to develop a catalyst support or work with a support manufacturer to achieve this. In industry, catalyst manufacturers either form symbiotic relationships with support manufacturers or become experts in support design and manufacture themselves. There have been a number of industrial acquisitions and joint ventures formed to exploit just such a relationship.

Preparation and Manufacture

The performance of a catalyst often depends as much on the care and method of preparation as on the identity of the active components. This fact has been learned by many who have failed to obtain reproducibility among catalyst preparations in the laboratory or have been responsible for quality assurance in catalyst manufacture. Also, there are many examples of strong effects of trace impurities in raw material or catalyst support on catalyst performance. Such trace impurities can actually determine the activity or selectivity of a catalyst. However, this serious problem in catalyst reproducibility can also offer leads toward discovery of new catalytic species, and a promising area of catalyst research involves ferreting out which active trace impurities are determining the performance of established catalysts.

Catalyst Preparation Methods. Excellent reviews of catalyst preparation and manufacture are available (13,22–26). The most common methods used to prepare supported catalysts include extruding, tableting, or pelletizing physically mixed (comulled) solid components, and impregnation of porous, shaped support bodies with the catalyst components dissolved in a solvent, usually water. In addition, some catalysts are produced and used as powders, granules, and the like. The details of most manufacturing methods for industrial catalysts are closely held secrets. Many hydrotreating and hydrogenation catalysts are examples of catalysts prepared by impregnation methods.

There are other methods of preparation that involve establishing an active phase on a support phase, such as ion exchange, chemical reactions, vapor deposition, and diffusion coating (26). For example, of the two primary types of propylene polymerization catalysts containing titanium supported on a magnesium halide, one is manufactured using wet-chemical methods (27) and the other is manufactured by ball milling the components (28).

Catalysts from Physical Mixtures. Two separate catalysts with different functions may be pulverized to fine powders and mixed to form a catalyst system that accomplishes a reaction sequence that neither of the two individual catalysts alone can achieve. For such catalyst systems, the reaction products of catalyst A become the feedstocks for catalyst B and vice versa. An example is the three-step isomerization of *n*-C₄+ alkanes by a mixture of supported platinum (catalyst A) and acidified alumina (catalyst B). The reaction sequence is initiated by dehydrogenation of the alkane to hydrogen and one or more alkenes on catalyst A. This is followed by isomerization of the alkene(s) on catalyst B and hydrogenation of the now-branched alkene on catalyst A. The net result is a one-reactor stage process that otherwise would have required three separate stages to accomplish. In a refinement of this concept, platinum may be supported on acidified alumina to form a dual-function catalyst that accomplishes the same result with greater efficiency.

Two or more solid catalyst components can be mixed to produce a composite that functions as a supported catalyst. The ingredients may be mixed as wet or dry powders and pressed into tablets, rolled into spheres, or pelletized, and then activated. The promoted potassium ferrite catalysts used to dehydrogenate ethylbenzene in the manufacture of styrene or to dehydrogenate butanes in the manufacture of butenes are examples of catalysts manufactured by pelletization and calcination of physically mixed solid components. In this case a potassium salt, iron oxide, and other ingredients are mixed, extruded, and calcined to produce the iron oxide-supported potassium ferrite catalyst.

When catalysts are used in a highly exothermic reaction, an active phase may be diluted with an inert material to help dissipate heat and moderate the reaction. This technique is practiced in the commercial oxychlorination of ethylene to dichloroethane, where an alumina-supported copper halide catalyst is mixed with a low surface area inert diluent.

Impregnated Catalysts. Preparation of impregnated catalysts usually involves filling the pore structure of a shaped, porous support body with a solution of the catalyst component(s), removing the solvent, and activating the catalyst. The impregnating solution may be a simple water solution of one or more soluble salts of the metal(s) and counterions to be deposited, or it may be a complex mixture incorporating solubilizing agents and or reactants, such as reducing agents that function during an activation step. An example of a complex impregnating solution is one used to prepare silver-based catalysts for the production of ethylene oxide. The solution contains a high concentration of a silver carboxylate in water and one or more organic amines that act to dissolve the silver salt and initiate reduction (29).

Dry Impregnation. In the so-called dry impregnation method, the amount of solution added to the solid support is exactly that calculated to completely fill the pores of the support. The solution may be sprayed onto the support in a blending operation and usually is absorbed quickly because of capillary action. The resulting mixture appears dry to the eye, thus the name dry impregnation has been applied. This method works well with supports that have relatively large, open-ended pores, even with aqueous solutions having a relatively high surface tension. Careful attention must be paid to the viscosity of the solution, which affects how much solution can be absorbed by the solid. Certain hydrotreating catalysts containing transition metals on alumina are examples of the use of this manufacturing method.

Pore Volume Impregnation. For catalyst supports with extremely small pores or a closed-end pore structure, it may be difficult to fill the support completely with impregnating solution by the dry impregnation method. In this case, immersion of the support in a solution containing the catalytically active components usually is more effective. Unless the solvent used has a high vapor pressure or contains dissolved gases, a complete pore volume impregnation usually can be aided by the use of vacuum. In this case, the bare support is placed in a suitable vessel, the air is withdrawn, and sufficient solution is introduced to cover the support while it is under vacuum. Air, or in some cases another gas, is then admitted to the vessel until at least atmospheric pressure is established, which forces the liquid into the evacuated pore structure of the support. Excess liquid is drained from the wet support and the excess solution is discharged. Liquids are removed from the impregnated support by controlled heating with or without the use of reduced pressure. Depending on the nature of the finished catalyst, the impregnated support may or may not be treated further or calcined in subsequent steps.

Since the goal in catalyst manufacture usually is to obtain a uniform dispersion of active species throughout the pore structure of the support, care must be taken to avoid deposition of different components on separate locations within the support. This can occur if during impregnation one of the components is more strongly adsorbed on the surface of the support than others, which can lead to enrichment of the strongly adsorbed component on the exterior surfaces of the catalyst and enrichment of the less strongly adsorbed components on the interior surfaces of the catalyst. This effect sometimes can be observed as a series of colored bands or concentric circles across the face of a broken catalyst particle and can be quantified by applying analytical techniques such as scanning electron microscopy (SEM) with elemental mapping. This type of problem can sometimes be alleviated by changing the composition of the support, the impregnating solution, or the time allowed for impregnation.

Preferential deposition of weakly adsorbed dissolved components on the outer surface of the catalyst body is a similar phenomenon but can occur after impregnation during removal of the solvent. When the impregnated particle is heated, the liquid phase expands and coats the exterior surfaces with dissolved species as the solvent evaporates. In particularly severe cases, the entire outer surface of the catalyst can become completely coated with a solid that blocks access to the underlying pore structure.

Ion-Exchange Catalysts. Catalytically active species can be deposited predictably and reproducibly on support materials capable of ion exchange to produce useful catalysts. The support can be organic, as in the case of ion-exchange resins or inorganic, as in the case of zeolites, which are by far the largest application for ion-exchange methods. The catalysts manufactured employing zeolites and their applications provide excellent examples of basic catalytic principles.

Zeolites, or molecular sieves, are highly structured crystalline aluminosilicates that occur both in nature and as synthetic products of sol-gel technology (12). The important natural zeolites are faujasite [12173-28-3], mordenite [12173-98-7], and erionite [12150-42-8], which provided the original structural models for zeolite synthesis. Early synthetic molecular sieve zeolites A, X, and Y were developed by Union Carbide Corp. in the 1950s and 1960s for use in gas purification and separation but later found applications in catalysis, whereas the highly versatile ZSM-5 zeolite invented by Mobil Oil Corp. in the early 1970s was developed for its catalytic properties, which have proved to be very important in modern petroleum refining and petrochemical operations.

The structure of the high SiO₂–Al₂O₃ ratio or pentasil ZSM-5 zeolite [58339-99-4] is determined by its synthesis. In a typical preparation (30), a silica source, such as Aerosil, is added to an aqueous solution of tetrapropylammonium hydroxide, and to this sodium aluminate dissolved in concentrated aqueous sodium hydroxide is added with vigorous stirring. The gel that forms is stirred for six days at 150°C, after which it is washed several times to remove soluble salts, dried, and calcined at 550°C. The product at this point contains sodium at the exchangeable sites. To incorporate the acidity required for catalytic use, the sodium may be exchanged directly by contact with solutions of mineral acids or the ZSM-5 may be converted to the ammonium form by refluxing the powder in a 0.5 M solution of ammonium nitrate followed by calcination at 550°C to decompose the ammonium cation to gaseous NH₃ and H⁺, which remains supported on the ZSM-5 framework. The acid form of ZSM-5 (HZSM-5) has stoichiometry H_{2.9}Na_{0.1}Al₃Si₃O₁₉₂.

By virtue of its strong Brønsted acidity, HZSM-5 is able to effect numerous hydrocarbon conversions that begin with carbonium ion formation (18), such as *n*-paraffin cracking and aromatics isomerization. The molecular dimensions of the pore structure in the zeolite crystal structure provide selectivity by excluding large and branched molecules from most of the acid sites. The acidity of ZSM-5 can be modified by exchanging the sodium of the as-synthesized zeolite or the hydrogen of HZSM-5 with other metals, such as Mg, Ca, Ba, and La (31). The general order of acidity for the various versions is H⁺ > RE³⁺ > Group IIA²⁺ > Group IA⁺, where RE refers to the rare-earth (lanthanide) elements. The acidity modification of the metal-supported zeolites is the result of the different hydration states of the various cations.

Other catalytically active metals may be supported on zeolites to give catalysts useful for different reactions (12). Such metals may be deposited by ion exchange as well as the more conventional techniques described earlier, but ion exchange frequently is preferred for preparing catalysts with low metal loadings. The metals useful in zeolite-supported hydrogenation catalysts include the appropriate Group (VIII) elements; those used in oxidation reactions include vanadium, chromium, manganese, molybdenum, tungsten, and silver. In a typical ion-exchange preparation, the ammonium form of the zeolite is allowed to equilibrate with a solution containing the metal in cationic form. For nickel, the solution could contain almost any soluble, neutral salt; for palladium or platinum this could be the ammonia complex, eg, Pd(NH₃)₄²⁺. To obtain the metals in the zero valent state, reduction with hydrogen or another reducing agent may be used.

Testing and Evaluation of Supported Catalysts

In the development phase of catalyst research, testing of the catalyst's chemical and physical properties and evaluation of the catalyst's performance are two essential tasks. In the manufacturing process, many of the same analyses and evaluations are used for quality assurance. A number of the testing procedures outlined earlier for catalyst supports can also be applied to catalysts (32).

Composition. The results of elemental analyses are almost always included among the specifications for a commercial catalyst. Depending on the accuracy desired and whether or not the catalyst can be rendered soluble without great difficulty, elemental analysis may be performed by x-ray methods, by one of the procedures based on atomic absorption, or by traditional wet-chemical methods. Frequently it is important to determine and report trace element components that may have an effect on catalyst performance.

Occasionally, especially in the developmental phase of catalyst research, it is necessary to determine the oxidation state, exact location, and dispersion of various elements in the catalyst. For these studies, either transmission electron microscopy (TEM) or scanning electron microscopy (SEM) combined with various high vacuum x-ray, electron, and ion spectroscopies are used routinely.

Surface Area. Overall catalyst surface area can be determined by the BET method mentioned earlier, but more specific techniques are required to determine a catalyst's active surface area. X-ray diffraction techniques can give data from which the average particle size and hence the active surface area may be calculated. Or, it may be necessary to find an appropriate gas or liquid that will adsorb only on the active surface and to measure the extent of adsorption under controlled conditions. In some cases, it may be possible to measure the products of reaction between a reactive adsorbent and the active site. Radioactively tagged materials are frequently useful in this application. Once a correlation has been established between either total or active surface area and catalyst performance (particularly activity), it may be possible to use the less costly method for quality assurance purposes.

Porosity and Pore Size. The same methods used to determine the porosity and pore size distribution of the support generally can be used for the catalyst. However, the values found for the catalyst usually are different from those of the bare support. Porosity could be increased if a part of the support is leached away during preparation of the catalyst, or, more likely, porosity will be decreased because catalytic materials deposited on the support will occupy a part of the support's pore volume.

Bulk Density. Measurements of bulk density for finished catalysts are similar to those on catalyst supports. Catalyst bulk density determinations can be one of the primary measures of consistency during catalyst manufacture. Care must be taken to specify whether loose bulk density or compacted (tapped) bulk density is being used. Loose bulk density is determined by measuring the weight of catalyst poured reproducibly into a container of known volume, whereas compacted bulk density seeks to determine the maximum amount of catalyst that will fit into a known volume by vibrating or tapping the container during filling.

Strength. Catalysts and supports must be sufficiently robust to withstand operations such as tumbling, pouring, and dropping without fracturing or dusting excessively, both of which can cause increased pressure drop and reactant maldistribution in a refining or chemical process catalyst bed. Often, a catalyst body will have to drop more than 10 m during loading into a reactor, and it must survive intact both the fall and the impact of other catalyst bodies falling on top of it.

Catalyst or support strength frequently is measured by a flat plate crush test in which an applied force is increased at a steady rate until the catalyst or support body fractures. The test may be applied to individual catalyst bodies, such as tablets, cylinders, pellets, or rings, or to a container of bodies, such as spheres, granules, and beads. For tests on individual bodies, a tablet is premeasured for length and placed between two polished flat plates, which are forced together in a small hydraulic or electrically driven press until the tablet breaks or deforms. The force required to break the tablet is read from a gauge. The results of several determinations are averaged and reported in terms of force/length.

For irregular or spherical bodies, a cylindrical container is loaded with a 100 gram or larger sample and a pistonlike cover is placed on top of the sample. The container is placed in a hydraulic press and a predetermined amount of force is applied to the cover at a controlled rate. The sample is removed from the container and screened to remove crushed particles (fines). The bulk crush strength is reported in terms of percent fines generated by a specified force.

Attrition Loss. In a commercial reactor, excessive catalyst attrition is very damaging and can cause the shutdown of the unit because of plugging in downstream equipment, increased pressure drop in the reactor, or reactant maldistribution, which can result in abnormal temperature gradients. Attrition can occur as a result of vibration or by the action of high gas velocities within the catalyst bed, but it can be minimized if sufficient attention is paid to this property during catalyst design, manufacture, and reactor loading.

Attrition loss is determined by loading a 100 g or larger sample of the support into a closed metal cylinder equipped with a baffle welded along the length of the inside surface of the cylinder such that when the cylinder is rolled the baffle lifts the sample and drops it once for every revolution of the cylinder (33). After the sample is rolled for a prescribed number of revolutions, it is removed from the cylinder, screened to separate the remaining whole bodies from the fines, and the weight percent of the original sample converted to powder is determined by weighing both fractions. Attrition loss is frequently included in the support specifications and is reported in terms of percent fines generated under specified conditions.

Performance Evaluation. Successful catalyst development requires a satisfactory means to determine the performance of the catalyst. The only significant proof of improvement in catalyst performance lies in evaluation in a reactor under the proper conditions.

One goal of catalyst designers is to construct bench-scale reactors that allow determination of performance data truly indicative of performance in a full-scale commercial reactor. This has been accomplished in a number of areas, but in general, larger pilot-scale reactors are preferred because they can be more fully instrumented and can provide better engineering data for ultimate scale-up. In reactor selection thought must be given to parameters such as space velocity, linear velocity, and the number of catalyst bodies per reactor diameter in order to properly model heat- and mass-transfer effects.

The advantages of using microreactors requiring only a few grams of catalyst sample include lower reactor costs, easier preparation of catalyst samples, conservation of expensive materials or raw materials from a single, uniform lot, and the possibility of installing many reactors in a relatively small area. This can make it possible to operate more than one reactor with a common feedstock source using one computer or control system and to monitor the product output using a single, on-line analytical instrument. In addition, it is possible to connect a very small pulse reactor directly to the inlet of a gas chromatographic analyzer and to feed the reactor with individual syringe injections (34).

Catalysts intended for different applications may require their own unique types of reactor and operating conditions, but the key to designing a successful system is to use the same feedstock composition that is expected in the ultimate commercial installation and to impose so far as is possible the same operating conditions as will be used commercially (35). This usually means a reactor design involving a tubular or small-bed reactor of one type or another that can simulate either commercial multitubular reactors or commercial-size catalyst beds, including radial flow reactors.

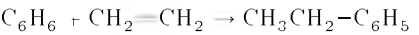
Deviations from the ideal frequently occur in order to avoid system complexity, but differences between an experimental system and the commercial unit should always be considered carefully to avoid surprises on scale-up. In the event that fundamental kinetic data are desired, it is usually necessary to choose a reactor design in which reactant and product concentration gradients are minimized (36), such as in the recycle (37) or spinning basket reactor designs (38,39).

The data most frequently collected and reported in catalyst performance evaluations are activity or turnover number, selectivity to the desired product(s), overall yield, catalyst life, and the identities and yields of by-products produced. These data are used to further catalyst or process development research efforts, to monitor catalyst manufacture, and to provide quality assurance information to catalyst users.

Applications of Supported Catalysts

There is an enormous volume of literature available on the applications for supported catalysts. Examples are compiled here based on important synthesis methods and industrial uses. The organization is according to specific reactions and applications rather than according to catalyst type.

Alkylation. An excellent example of alkylation is the Mobil-Badger process, which uses ZSM-5-type zeolite to produce ethylbenzene by alkylation of benzene with ethylene (12,40):

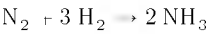


In this application, ZSM-5 acts as a strong, solid acid, and may be viewed as H+ supported on the surfaces of the crystalline zeolite structure. The older, Friedel-Crafts aluminum chloride catalyzed process for ethylbenzene produces considerably more by-products and suffers from the corrosivity of the catalyst system. Because of the intermediate pore size of ZSM-5, those reactions that produce coke from larger molecules that cannot enter the ZSM-5 pore structure are significantly reduced, which greatly extends catalyst lifetime.

The same type catalyst modified with boron (41), magnesium (42), or phosphorus (43) to reduce the pore size can be used to alkylate toluene with ethylene to produce predominantly *p*-ethyltoluene. Since *p*-ethyltoluene [622-96-8] has the smallest effective diameter of the ethyltoluene isomers, the selectivity to this isomer is favored because it can most easily escape the ZSM-5 pore structure. For the same reason, the alkylation of toluene [108-88-3] to *p*-xylene [106-42-3] also is favored over the usual acid catalyzed equilibrium mixture of isomers when it is carried out over magnesium- or phosphorus-modified ZSM-5 (44).

Catalysts in the ZSM-5 and ZSM-11 family are used to convert methanol into high octane gasoline components in the Mobil MTG process (45). The conversion proceeds through dimethyl ether as an intermediate and the products are paraffins, aromatics, cycloparaffins, and C+olefins, all of which must involve alkylation reactions catalyzed by the strong acid function of the zeolite. This technology represents a significant advancement in the potential for using coal as a raw material for gasoline and hydrocarbons.

Ammonia Synthesis. Ammonia (qv) has been manufactured by the hydrogenolysis of the N-N bond in nitrogen over an iron-based catalyst since the beginning of the twentieth century (46):



Over the years, literally thousands of catalyst formulations have been evaluated and those available today are significantly more active, which has allowed considerable improvement in productivity and plant operation. Today, a typical catalyst contains approximately 93 wt % Fe3O4, and about 1 wt % potassium oxide, 3 wt % alumina, 3 wt % calcium oxide, and 0.5 wt % silica, which is actually an unnecessary impurity.

Research in catalysts for ammonia manufacture is still going on, and though the use of supported metals such as ruthenium may be two to three times as active as promoted iron oxide, catalysts 50–100 times more active than promoted iron oxide are required to affect process economics significantly.

Catalytic Cracking. The catalytic cracking unit in a modern oil refinery produces gasoline range hydrocarbons from long-chain, higher boiling fractions of crude oil and the product of coker units. The reactions that occur convert paraffins, alkyl naphthenes, and alkyl aromatics to olefins plus shorter chain-length paraffins, naphthenes, and aromatics, respectively. The catalysts of choice for catalytic cracking are various modifications of the large pore Y zeolites (faujasites) chosen for this application because of superior thermal and hydrothermal stability. They are commonly incorporated into what are called fluid catalytic cracking catalysts, or FCC catalysts.

When zeolites were introduced into catalytic cracking in 1962, they replaced synthetic amorphous silica–aluminas and revolutionized the cracking operation by virtue of their selectivity to gasoline range hydrocarbons and their extremely high activity, at least 10⁴ times as active, when in the H form, as the silica–aluminas they replaced (40). To make optimum use of the high activity and selectivity of zeolites, FCC catalysts utilize a largely inert silica–alumina support matrix, which acts to dilute the active zeolite, provide a macroporous structure, and give the granular catalyst increased strength and resistance to abrasion. Without the matrix, zeolites would not be able to process large molecules and would lose selectivity by overcracking. The catalyst must survive both the 480–520°C cracking environment and a regeneration environment, in which coke formed on the catalyst is burned off with air under controlled conditions at 595–675°C (see CATALYSTS, REGENERATION).

The silica–alumina matrix phase in an FCC catalyst is generated by hydrogel precipitation techniques and comprises 60–90 wt % of the catalyst. Small (1–5 micrometer) particles of the zeolite are mixed with the gel prior to spray drying. The spray-dried granules are washed and flash dried to produce a 50–60 micrometer diameter finished catalyst. The Y zeolite used in FCC applications is manufactured in the sodium Y form, stabilized, and converted to an acid form, such as hydrogen Y, stabilized hydrogen Y, rare-earth Y, rare-earth hydrogen Y, calcined rare-earth Y, and magnesium rare-earth Y (40). The rare-earth modification replaces sodium with predominantly lanthanum, neodymium, and praseodymium, and confers additional stability to the zeolite structure. The properties required in an FCC catalyst are (1) high cracking activity; (2) high selectivity to gasoline as opposed to gas and coke; (3) hydrothermal stability; (4) resistance to attrition; and (5) resistance to poisoning by metals especially nickel, vanadium, and sodium. The parameters used to achieve these properties include the type and fraction of the zeolite in the catalyst, and the composition and properties of the matrix.

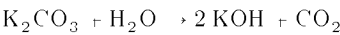
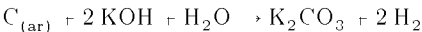
In addition to the conventional analytical techniques cited earlier for catalysts in general, information concerning bonding and species present within and outside of the crystal lattice in FCC catalysts and zeolites in general can be obtained from ²⁹Si and ²⁷Al magic angle spinning nmr measurements, which allow chemical shifts to be determined on solids (47). Evaluation of FCC catalysts frequently is carried out using a microactivity test set up very much like a pulse reactor attached to a gas chromatograph, and only very small samples are required for analysis (48).

Dehydrogenation. Dehydrogenation processes are used extensively in the production of styrene and butadiene from ethylbenzene and 1-butene, respectively. Both processes use promoted potassium ferrite [12022-41-2], KFeO₂, supported on iron oxide. The catalysts used to manufacture styrene typically are prepared by combining iron (III) oxide and or hydrated iron (III) oxide with a potassium salt, water, and a promoter package that may contain a salt or oxide of a group (IIA) metal, eg, magnesium and or calcium, and a Group (VB) or (VIB) metal, eg, vanadium, chromium, molybdenum, or tungsten. The solid ingredients are mixed thoroughly with sufficient water to form a plastic mass that can be extruded or pelletized and then calcined at a temperature of 400°C or higher. Potassium ferrite is formed during the high temperature calcination and can be identified by its characteristic x-ray diffraction pattern. At the same time, the potassium salts of the Group (VB VIB) metals are formed.

In most existing styrene processes, the catalyst is loaded into large, radial flow reactors, which are operated adiabatically at low pressure and temperatures near 600°C. Heat is supplied by superheated steam. During start-up, dehydrogenation begins slowly and accelerates as the Fe (III) is reduced to Fe (II,III). The catalyst, which was red in color when fresh, turns to the characteristic black color of Fe₃O₄.

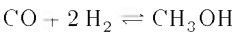
The feedstocks to the styrene process are ethylbenzene and superheated steam, and a typical unit produces hydrogen, small amounts of light hydrocarbons and carbon dioxide as gaseous products, and a liquid product stream containing 95% + styrene and minor amounts of toluene, benzene, and other aromatics. In an integrated plant, the benzene can be recycled to the ethylbenzene unit, while the other by-products usually are consumed as fuel for the highly endothermic process.

Dehydrogenation is considered to occur on the corners, edges, and other crystal defect sites on the catalyst where surface vacancies aid in the formation of intermediate species capable of competing for hydrogen with ethylbenzene. The role of the potassium may be viewed as a carrier for the strongly basic hydroxide ion, which is thought to help convert highly aromatic by-products to carbon dioxide.



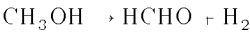
Catalysts that do not contain potassium lose activity very quickly because of coke deposition on the surface of the catalyst. Chemical changes that occur when the catalyst is removed from the operating environment make it very difficult to determine the nature of most of the promoter elements during the reaction, but potassium is always found to be present as potassium carbonate in the used catalyst. The other promoters are claimed to increase selectivity and the operating stability of the catalyst.

Another dehydrogenation of interest can be used to generate very pure hydrogen for hydrogenation reactions and involves the following equilibrium



which can be made to proceed either to the left by the use of higher temperatures and lower pressures or to the right by the use of lower temperatures and higher pressures (49). Copper and zinc oxides on alumina can be used in this reaction.

In the presence of metallic copper, metallic silver, or a copper-silver alloy used in the form of gauze or as metal deposited on a low surface area inert support, methanol can be dehydrogenated to formaldehyde at 400–500°C.



Although this pure dehydrogenation reaction is not practiced commercially, at least two processes exist in which methanol is dehydrogenated to formaldehyde in the presence of air.

Cyclohexane can be dehydrogenated to benzene very cleanly under the same conditions with the same copper-silver catalyst, as can 2-propanol to acetone. These catalysts almost certainly act by virtue of an oxide layer on the metal.

Some of the same dehydrogenation reactions can be effected in an oxidative mode over a supported bismuth molybdate or iron molybdate catalyst. In such oxidative dehydrogenation processes, air is injected with the main reactant to effect combustion of the hydrogen produced to generate heat and to help shift the equilibrium toward the dehydrogenated product. In a variation of oxidative dehydrogenation, the dehydrogenation and oxidation steps can be separated, as in the Lummus-Crest Styro-Plus styrene process. Here, oxygen is injected into a small hydrogen oxidation reactor located between two ethylbenzene dehydrogenation stages and is used to burn the hydrogen produced in the upstream reactor over a supported catalyst containing a precious metal. The combined effects of removing the hydrogen and reheating the feed to the downstream reactor is claimed to improve process economics by about 15%.

Emission Control Catalysts.

Automotive Catalytic Converter Catalysts. California environmental legislation in the early 1960s stimulated the development of automobile engines with reduced emissions by the mid-1960s, led to enactment of the Federal Clean Air Act of 1970, and resulted in a new industry, the design and manufacture of the automotive catalytic converter (50). Between 1974 and 1989, exhaust hydrocarbons were reduced by 87% and nitrogen oxides by 24%.

The requirements of the Clean Air Act and its amendments have been met by the development of the catalytic converter, which is designed to reduce the concentrations of unburned hydrocarbons, carbon monoxide, and nitrogen oxides in auto exhaust, and by government mandated elimination of lead and phosphorus from engine fuels by the oil industry. The catalytic converter, however, is only one part of the emissions system. The adoption of lower compression engines operating close to the stoichiometric fuel-air mixture and computer controlled ignition timing guided by measurement of the oxygen content of the exhaust gas has made the task of the catalytic converter considerably easier. The use of fuel injected engines has also lowered the amount of unburned hydrocarbons entering the exhaust system.

In principle, the catalytic converter is a fixed-bed reactor operating at 500–620°C to which is fed 200–3500 liters per minute of auto engine exhaust containing relatively low concentrations of hydrocarbons, carbon monoxide, and nitrogen oxides that must be reduced significantly. Because the auto emission catalyst must operate in an environment with profound diffusion or mass-transfer limitations (51), it is apparent that only a small fraction of the catalyst's surface area can be used and that a system with the highest possible surface area is required.

In the development of the catalytic converter there have been two competing catalyst support systems, one that relied on conventional pellet support technology developed by General Motors and another based on the independent development of the multichanneled monolithic support by 3M and Corning Glass. Both systems rely on a thermally stable support, alumina spheres in one case and corderite multichanneled monolithic logs in the other. Both are relatively low in surface area as a result of the need to calcine the bodies at high temperatures for mechanical strength.

To add surface area, the supports are uniformly coated with a slurry of gamma-alumina and recalcined under moderate conditions. The wash coat acts to accept the active metals, typically low levels of platinum and palladium, in a conventional impregnation process. In the United States in passenger car applications the spherical catalyst is used almost exclusively, and methods have been developed to replace the catalyst without removing the converter shell when vehicle inspection reveals that emission standards are not met.

NO_x Reduction in Stack Gases. Nitrogen oxides in the stack gas of power plants react with ammonia to form nitrogen and water over a supported vanadium pentoxide catalyst. This is a large-scale worldwide practice. W. R. Grace offers the SYNOX catalyst using high surface area vanadia and titania for this application. These oxides tend to sinter badly and lose surface area at high temperatures and it is necessary to create a system in which their surface areas are stabilized. This is accomplished by dispersing TiO₂ on high surface area silica and then depositing V₂O₅ on the titania.

The first commercial application of precious metals for the reduction of nitrogen oxides in power plant emission control was in 1989. W. R. Grace's

CAMET control catalyst was shown to obtain 80° o NO_x reduction and 95° o carbon monoxide reduction in this application in the Santa Maria, California cogeneration project. The catalyst consists of a corrugated metal substrate onto which the active noble metal is evenly deposited with a washcoat. Unlike the typical V₂O₅ on titania turbine exhaust catalysts used earlier in these applications, the CAMET catalyst is recyclable (52).

Hydrocarbons from Synthesis Gas and Methanol. Two very important catalytic processes in which hydrocarbons are formed from synthesis gas are the Sasol Fischer-Tropsch process, in which carbon monoxide and hydrogen obtained from coal gasification are converted to gasoline and other products over an iron catalyst, and the Mobil MTG process, which converts methanol to gasoline range hydrocarbons using ZSM-5-type zeolite catalysts.

Sasol Fischer-Tropsch Process. The Fischer-Tropsch process for gasoline and diesel fuel production has been in continuous operation by Sasol in South Africa since 1955. Numerous improvements have been made to the German-licensed process over the years, and capacity has been increased several times. Synthesis gas produced from low-grade coal in Lurgi dry ash gasifiers, which produce a raw product containing 60 mol ° carbon monoxide and hydrogen, is purified to an 85 mol ° content stream in the Lurgi Rectisol process (53).

Sasol uses both fixed-bed reactors and transported fluidized-bed reactors to convert synthesis gas to hydrocarbons. The multitubular, water-cooled fixed-bed reactors were designed by Lurgi and Ruhrchemie, whereas the newer fluidized-bed reactors scaled up from a pilot unit by Kellogg are now known as Sasol Synthol reactors. The two reactor types use different iron-based catalysts and give different product distributions.

The fixed-bed catalyst is a silica-based extrudate containing precipitated iron oxide promoted with potassium and copper. The catalyst is activated by hydrogen reduction of most of the iron catalyzed by small amounts of copper. As the catalyst is used, additional reduction occurs and Hagg carbide [12127-45-6], Fe₅C₂, is formed.

In the fluidized-bed reactors, the catalyst is transported at high velocities and must have high strength to avoid attrition. This catalyst is manufactured in powder form by fusing together the iron oxide and promoters in an electrical furnace. Among the useful promoters to impart strength to the catalyst are aluminum oxide, magnesium oxide, titanium dioxide, and chromium (III) oxide, all of which form spinel structures with the iron (II,III) oxide. Potassium is used to enhance activity and selectivity. The large pieces produced are pulverized to a fine powder suitable for use in the transportable-bed reactors. This catalyst also must be reduced with hydrogen prior to use.

Although the product mix changes with catalyst age and also can be altered by changing the process conditions, in general the C₅–C₁₁ gasoline range product from the fixed-bed reactor contains more paraffins (60° o vs 14° o) and fewer olefins (32° o vs 57° o) than the fluidized-bed reactor, which also makes up to 7° o aromatics while the fixed-bed reactor makes none (53). In the fluidized-bed plant operated at 325°C, the gasoline range hydrocarbons make up 40° o of the product, compared with only 18° o in the fixed-reactor plant operated at 220°C, where the main products are C₂₄+ waxes (45° o).

Mobil Methanol to Gasoline (MTG) Process. As with the Fischer-Tropsch process, Mobil's MTG process can be operated as a fixed-catalyst-bed reactor or a fluid bed (54). The first stage dehydrates methanol to dimethyl ether, which is converted to hydrocarbons and water over a ZSM-5-type zeolite catalyst. The strong acid character of ZSM-5 catalyzes the conversion of dimethyl ether to light olefins, which undergo oligomerization to heavier products, including paraffins and aromatics. The medium pore size ZSM-5-type zeolite is essential to this process, since a smaller pore size requires more severe operating conditions and does not produce aromatics, whereas larger pore-size zeolites produce heavy aromatics, which form coke deposits rapidly and deactivate the catalyst. The shape selective nature of ZSM-5 limits the size of the hydrocarbons produced to predominantly C₁₀ and below.

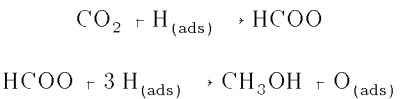
Hydrogenation. Hydrogenation is one of the oldest and most widely used applications for supported catalysts, and much has been written in this field (55–57). Metals useful in hydrogenation include cobalt, copper, nickel, palladium, platinum, rhenium, rhodium, ruthenium, and silver, and there are numerous catalysts available for various specific applications. Most hydrogenation catalysts rely on extremely fine dispersions of the active metal on activated carbon, alumina, silica-alumina, zeolites, kieselguhr, or inert salts, such as barium sulfate.

Methanol Synthesis. Methanol has been manufactured on an industrial scale by the catalyzed reaction of carbon monoxide and hydrogen since 1924. The high pressure processes, which utilize zinc oxide–chromium oxide catalysts, are operated above 20 MPa (200 atm) and temperatures of 300–400°C. The catalyst contains approximately 72 wt ° zinc oxide, 22 wt ° chromium (II) oxide, 1 wt ° carbon, and 0.1 wt ° chromium (VI); the balance is materials lost on heating.

Although copper catalysts were known to be highly active for this reaction for many years, it was not until the late 1960s that gas purification processes for synthesis gas were introduced that would allow the commercial use of these catalysts, which require very low sulfur, chlorine, and phosphorus feed impurity levels to maintain catalyst activity.

The dominant process in modern methanol manufacture is the ICI low pressure process (58). Because of the potentially huge market for methanol as an automotive fuel, this technology is an extremely important application for supported catalysts. The ICI process uses a catalyst typically formed as 5 mm × 5 mm cylinders containing copper, zinc, and aluminum precipitated simultaneously as the oxides. The copper oxide must be reduced to copper metal prior to use, and in order to obtain a high copper surface area, reduction is carried out slowly using hydrogen diluted with an inert gas at temperatures <300° C. A copper content of about 60 wt ° is optimum. To avoid the loss of copper surface area by processes similar to sintering during operation, the temperature limit for use of this type catalyst is about 270°C.

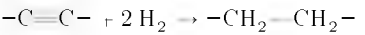
Only recently has a mechanism been proposed for the copper-catalyzed reaction that is completely satisfactory (58). It had been known for many years that a small amount of carbon dioxide in the feed to the reactor is necessary for optimum yield, but most workers in the field believed that the main reaction in the formation of methanol was the hydrogenation of carbon monoxide. Now, convincing evidence has been assembled to indicate that methanol is actually formed with >99% selectivity by the reaction of dissociated, adsorbed hydrogen and carbon dioxide on the metallic copper surface in two steps:



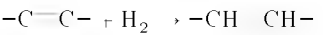
The adsorbed oxygen atom on the copper surface is removed by reaction with carbon monoxide and provides a pathway for the formation of the carbon dioxide needed in the main reaction.

The predominate role of the zinc and aluminum oxides in the ICI catalyst is to reduce the rate of sintering and loss of metallic copper surface area, which, in addition to poisoning, is one of the modes of activity loss with time for this catalyst.

Hydrogenation of Acetylenes. Complete hydrogenation of acetylenes to the corresponding alkanes, which may be required to remove acetylenic species from a mixture, or as a part of a multistep synthesis, may be accomplished using <5 wt % palladium or platinum on alumina in a nonreactive solvent under very mild conditions, ie, <100° C, <1 MPa (10 atm). Platinum is preferred in those cases where it is desired to avoid isomerization of the intermediate olefin. Silver on alumina also can be used in this application as can unsupported platinum metal.



Most refinery petrochemical processes produce ethylene that contains trace amounts of acetylene, which is difficult to remove even with cryogenic distillation. Frequently it is necessary to lower the acetylene concentration from several hundreds ppm to <10 ppm in order to avoid poisoning catalysts used in subsequent ethylene consuming processes, such as polymerization to polyethylene. This can be accomplished with catalytic hydrogenation according to the equation.



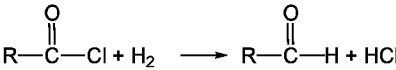
Since both complete hydrogenation of acetylene or any hydrogenation of the ethylene results in the production of a less valuable product such as ethane, conditions must be chosen carefully and a catalyst must be used that is both sufficiently active for acetylene hydrogenation and extremely selective to avoid ethylene hydrogenation. Since hydrogenation of acetylenic bonds proceeds stepwise and since acetylene is more strongly adsorbed on the catalytic

site than ethylene, it is possible to accomplish the partial hydrogenation with high selectivity to ethylene by using mild conditions and a low catalyst to substrate ratio. Catalysts containing palladium supported on alumina are available for this application.

The presence of other functional groups in an acetylenic molecule frequently does not affect partial hydrogenation because many groups such as olefins are less strongly adsorbed on the catalytic site. Supported palladium catalysts deactivated with lead (such as the Lindlar catalyst), sulfur, or quinoline have been used for hydrogenation of acetylenic compound to (predominantly) cis-olefins.

Another application for this type catalyst is in the purification of styrene. Trace amounts (200–300 ppmw) of phenylacetylene can inhibit styrene polymerization and cannot easily be removed from styrene produced by dehydrogenation of ethylbenzene using the high activity catalysts introduced in the 1980s. Treatment of styrene with hydrogen over an inhibited supported palladium catalyst in a small post reactor lowers phenylacetylene concentrations to a tolerable level of <50 ppmw without significant loss of styrene.

Reduction of Acid Chlorides to Aldehydes. Palladium catalysis of acid chlorides to produce aldehydes is known as the Rosenmund reduction and is an indirect method used in the synthesis of aldehydes from organic acids.

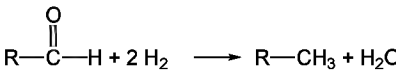


The catalyst commonly used in this method is 5 wt % palladium supported on barium sulfate inhibited with quinoline–sulfur, thiourea, or thiophene to prevent reduction of the product aldehyde. A procedure is found in the literature (57). Suitable solvents are toluene, benzene, and xylene used under reflux conditions. Interestingly, it is now thought that Rosenmund's method (59) originally was successful because of the presence of sulfur compounds in the xylene used, since the need for an inhibitor to reduce catalyst activity was not described until three years later (60).

Reduction of Aromatic Aldehydes and Ketones to Alcohols. Catalysts are available that can hydrogenate aromatic aldehydes and ketones to alcohols both with and without hydrogenating the aromatic nucleus. Catalysts containing 5 wt % rhenium, rhodium, or ruthenium supported on alumina or carbon used at higher pressures (1–5 MPa 145–725 psi) in nonpolar solvents are capable of complete saturation of the functional group and the ring at moderate temperatures of <100°C. In the case of aldehydes, significant reduction of the alcohol function to a methyl group may preclude achieving complete ring saturation.

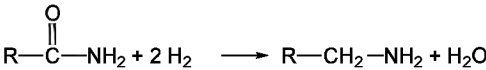
For more selective hydrogenations, supported 5–10 wt % palladium on activated carbon is preferred for reductions in which ring hydrogenation is not wanted. Mild conditions, a neutral solvent, and a stoichiometric amount of hydrogen are used to avoid ring hydrogenation. There are also applications for 35–40 wt % cobalt on kieselguhr, copper chromite (nonpromoted or promoted with barium), 5–10 wt % platinum on activated carbon, platinum (IV) oxide (Adams catalyst), and rhenium heptasulfide. Alcohol yields can sometimes be increased by the use of nonpolar (nonacidic) solvents and small amounts of bases, such as tertiary amines, which act as catalyst inhibitors.

Reduction of Aldehydes and Ketones to Hydrocarbons. Deep hydrogenation of aldehydes and ketones removes the oxygen functionality and produces the parent hydrocarbons.



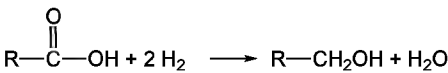
This reaction is favored by moderate temperatures (100–150°C), low pressures, and acidic solvents. High activity catalysts such as 5–10 wt % palladium on activated carbon or barium sulfate, high activity Raney nickel, or copper chromite (nonpromoted or promoted with barium) can be used. Palladium catalysts are recommended for the reduction of aromatic aldehydes, such as that of benzaldehyde to toluene.

Hydrogenation of Amides to Amines.



True supported catalysts are not favored for this reaction, but it can be effected by the use of finely divided rhenium metal or rhenium (VI) oxide as well as hydrated ruthenium (IV) oxide.

Reduction of Carboxylic Acids to Alcohols. In addition to the nonsupported catalysts mentioned for the hydrogenation of amides to amines, ruthenium and rhenium on alumina can be used to reduce carboxylic acids to alcohols. The conditions for this reduction are somewhat more severe than for most other hydrogenation reactions and require higher temperatures, >150°C, and pressures, >5 MPa (725 psi) (55). Various solvents can be used including water.



Hydrogenation of Aromatic Nitriles to Amines. Nitriles containing an aromatic nucleus can be converted to the corresponding amine with or without affecting the aromatic nucleus, depending on the catalyst used and the conditions chosen. Complete saturation of the functional group and the aromatic nucleus can be accomplished using 5 wt % rhodium on carbon and moderately severe conditions.

Supported palladium, zirconium-promoted cobalt on kieselguhr, or nickel on kieselguhr can be used under relatively mild conditions to effect reduction of the nitrile function without hydrogenating the ring.



An acidic solvent is recommended for use with palladium. Other catalysts that have been used for this reduction include copper chromite and any of the three Raney catalysts, cobalt, iron, or nickel.

Reduction of Aromatic Nitro Compounds to Aromatic Amines. Mild conditions and a large variety of catalysts effect reduction of aromatic nitro compounds to aromatic amines (see AMINES BY REDUCTION).



Palladium and platinum (5–10 wt % on activated carbon) can be used with a variety of solvents as can copper carbonate on silica and 60 wt % nickel on kieselguhr. The same is true of nonsupported catalysts copper chromite, rhenium (VII) sulfide, rhenium (VI) oxide, and any of the Raney catalysts, copper, iron, or nickel.

Hydrogenation of the Aromatic Ring. Most of the platinum group metals are capable of hydrogenating benzene to cyclohexane, though platinum and rhodium are preferred for use at mild conditions, and palladium and ruthenium are more useful at higher temperatures and pressures. Since olefinic intermediates are more easily hydrogenated than aromatics, they normally do not appear in the product if aromatic conversion is carried to completion; there are exceptions to this rule, however (55). The sensitivity of ring substituents and other functional groups to hydrogenolysis frequently affects the choice of catalyst. Other catalysts that may be used for aromatic ring reduction include cobalt molybdate on alumina, nickel on kieselguhr, nickel tungstate on alumina or silica alumina, Raney cobalt, iron and nickel, and hydrated ruthenium (VI) oxide.

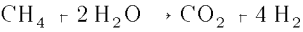
Hydrogenation of heteroaromatic rings may be carried out in solution using most of the platinum group metals, but rhodium on alumina or activated carbon is preferred in order to obtain satisfactory yields using heterogeneous catalysis. Frequently, the heteroatom in heteroaromatic rings acts as a ligand to the platinum group metal and in so doing reduces the activity of the catalyst.

Hydrotreating. Hydrotreating is a petroleum refining term for operations in which hydrogen is used to increase the utility or the value of a refinery stream. These operations include desulfurization, denitrogenation, hydrogenation, and hydrotreating. In addition, the term has been applied loosely to hydrocracking and to conversion of sulfur-containing compounds to hydrogen sulfide as practiced in the Claus process and a number of other, lower volume processes specific to certain types of crude oil feedstocks. An excellent review is available (61).

In the simplest case, in a modern petroleum refinery there are four large volume streams that utilize hydrotreating, and all four of these streams originate from distillation of crude oil at atmospheric pressure with further separation of the least volatile fractions by vacuum distillation. The four streams with their boiling ranges are naphtha (C₅ to 204°C), middle distillate (177–343°C), vacuum gas oil (343–566°C), and residual oil (>566°C). Since these streams have rather wide boiling ranges, they can be further separated into their components or narrower boiling fractions.

Desulfurization and Denitrogenation. Removal of sulfur- and nitrogen-containing compounds from feeds to catalytic cracking units, hydrocracking units, and reformers is necessary to avoid deactivation of the catalysts. These operations are termed desulfurization and denitrogenation and involve the hydrogenolysis of the C–S and C–N bonds to form hydrogen sulfide and ammonia, respectively, with consequent formation of saturated alkyl groups. Desulfurization and denitrogenation are carried out simultaneously using the same catalysts. Oxygen-containing compounds in the stream are deoxygenated at the same time by similar chemistry, and any alkenes present are converted to the corresponding alkane.

Hydrotreating units are large consumers of hydrogen, and the main source is the catalytic reforming unit where C + straight-chain hydrocarbons are converted to aromatics with concurrent production of hydrogen. Additional hydrogen can be supplied from natural gas or light hydrocarbons by steam reforming:



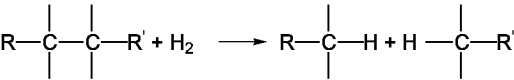
Hydrotreating units typically are large down flow or radial flow fixed-bed reactors, or ebullating- or expanded-bed reactors in which the catalyst is continuously added and withdrawn (62). The catalysts used in these operations are selected from a group that contain nickel- or cobalt-promoted molybdenum or tungsten supported on high surface area alumina. The metal levels in these catalysts are relatively high, such as 4–16 wt % Ni and 16–20 wt % W in a nickel-promoted tungsten catalyst.

Catalyst choice is strongly influenced by the nature of the feedstock to be hydrotreated. Thus, whereas nickel-promoted and cobalt–nickel-promoted molybdenum catalysts can be used for desulfurization of certain feedstocks and operating conditions, a cobalt-promoted molybdenum catalyst is generally preferred in this application. For denitrogenation and aromatics saturation, nickel-promoted molybdenum catalysts usually are the better choice. When both desulfurization and denitrogenation of a feedstock are required, the choice of catalyst usually is made so that the more difficult operation is achieved satisfactorily.

Hydrotreating catalysts are manufactured by comulling and impregnation methods and may be purchased presulfided or as calcined extrudate in the form of mixed oxides. When the oxide form is purchased, it must be sulfided in the hydrotreating reactor prior to use. This is accomplished by adding small amounts of a sulfiding agent such as dimethyl sulfide [75-18-3], dimethyl disulfide [24-92-0], or low molecular weight mercaptans to the initial feed to the hydrotreater. Feedstocks that tend to form coke on the catalyst surface, which is the main cause of deactivation for this type of catalyst, should be avoided during sulfiding.

Catalyst deactivation. Coke buildup on the catalyst is the main mode of deactivation, but other impurities also contribute to performance loss. Nickel and vanadium are present in porphyrins found in crude oils, and they accumulate on hydrotreating catalysts to the extent that, in some cases, a spent catalyst contains up to 30 wt % of the metals. Larger pore versions of hydrotreating catalysts frequently are used at the top of the bed to act as demetallization catalysts to extend catalyst-bed life. Lead and arsenic are two other problem impurities that poison these catalysts. Iron and sodium accumulation in the catalyst bed and in the catalyst pores contribute to reactor feed maldistribution and, secondarily, to deactivation by pore plugging. The degree of success for catalyst regeneration procedures in which coke is removed from the catalyst by controlled oxidation frequently hinges on the accumulated levels of metallic impurities that cannot be removed from the catalyst. After many cycles of use, when regeneration is no longer possible, the metals present in spent hydrotreating catalysts are reclaimed and recycled.

Hydrocracking. Hydrogenolysis of a carbon–carbon bond in an organic molecule produces smaller, hydrogen-saturated molecules and is termed hydrocracking when 50% or more of the feedstock is converted into smaller molecules.



An example of an application of hydrocracking is in lubricating oils, where it is used to improve the viscosity index, color, and color stability; to reduce polymer formation (storage stability); and to decrease the neutralization number (acidity) (61).

The same catalysts used in other hydrotreating operations are employed in hydrocracking. Mild hydrocracking is carried out using hydrogen pressures less than 6.5 MPa (940 psi), whereas true hydrocracking uses pressures greater than 10 MPa (1450 psi). Both are predominantly liquid-phase processes carried out in fixed-bed or ebullating-bed reactors using catalysts that typically contain nickel or cobalt, molybdenum, and phosphorus supported on gamma-alumina.

Catalytic dewaxing is another example of hydrocracking; however, this process makes use of the shape selective properties of zeolites to convert long-chain molecules to shorter fragments. Waxy, long-chain linear and slightly branched hydrocarbons are selectively hydrocracked, but aromatics, naphthenes, and highly branched paraffins are unaffected. The result is the pour point, cloud point, and freeze point of the product are decreased. The process is used in middle distillate dewaxing and in lubricating oil dewaxing as an alternative to solvent extraction. A nickel-containing ZSM-5-type catalyst is used in the Mobil Lube Dewaxing process; a similar British Petroleum process uses platinum supported on hydrogen mordenite (40).

Isomerization. Isomerization of low octane C₅ and C₆ *n*-paraffins in gasoline streams into higher octane branched isomers is an important refinery operation, since these materials are too low boiling and unsuitable to be enhanced by reforming. Shell Oil Company's Hysomer process operates with moderate hydrogen pressures at about 250°C and uses a catalyst containing a noble metal supported on a mordenite-type zeolite to obtain an octane number increase of about 12 (63). In an enhancement of this technology, Union Carbide's Total Isomerization process separates and recycles *n*-paraffins unconverted in their Isosiv process back to the isomerization unit to obtain an octane number increase of about 20 (40).

Another example of catalytic isomerization is the Mobil Vapor-Phase Isomerization process, in which *p*-xylene is separated from an equilibrium mixture of C₈ aromatics obtained by isomerization of mixed xylenes and ethylbenzene. To keep xylene losses low, this process uses a ZSM-5-supported noble metal catalyst over which the rate of transalkylation of ethylbenzene is two orders of magnitude larger than that of xylene disproportionation (12).

Reforming. Reforming is the refinery operation (64) in which naphthenes and C₆ + aliphatic hydrocarbons in naphtha feedstock are catalytically dehydrogenated and isomerized to increase the aromatics and branched-chain hydrocarbon content, which raises the octane number of the naphtha and increases its value as an internal combustion engine fuel. If desired, the aromatics produced, largely benzene, toluene, and xylene, can be separated and used as chemical process feedstocks (see BTX PROCESSING). The hydrogen produced in the reforming unit is utilized in hydrotreating operations. The catalyst used in this process typically contains 0.3–0.7% platinum and lesser amounts of other metals, such as rhenium or iridium, as well as, in various versions, 1 wt % or less of gallium, indium, germanium, tin, or lead, supported on chlorided (acidified) gamma-alumina. These bimetallic or multimetallic catalysts typically have surface areas in the range 175–300 m²/g and pore volumes in the range 0.45–0.65 cm³/g (65) and are considered dual function catalysts. They represent an improvement over earlier platinum on alumina catalysts in their ability to resist coke fouling when operated at low pressures. Dehydrogenation and hydrogenation occur on the active metal sites; isomerization takes place on the acidic alumina surface.

It is necessary for bimetallic catalysts used in reforming to operate with a reduced, sulfided surface. It is common practice to reduce and presulfide the catalyst in the reforming unit using hydrogen for reduction and a low concentration of a sulfur-containing compound such as hydrogen sulfide or dimethyl sulfide for sulfiding. Since excessive sulfiding acts to poison the catalyst, sulfur-containing compounds and other poisons must be removed from

the reformer feed in a prior hydrotreating operation. The activity of the chlorided alumina support that provides the acid function to the catalyst must be maintained in balance with the activity of the metal function for optimum performance. Chlorided alumina is sensitive to moisture, which can cause hydrolysis and loss of chloride, and for this reason care must be taken to avoid contact with moisture during catalyst handling and reactor loading. The catalyst is also sensitive to excessive chloride content in the reformer feed, which can over-chloride the surface. Paradoxically, activity balance can be maintained in these catalysts by intentionally adding small amounts of water or a chloride to the reformer feed to adjust the chloride level on the catalyst (65).

Reforming catalysts eventually lose activity by accumulation of coke, but regeneration is possible by carefully burning the coke off the catalyst with oxygen. Regeneration can be accomplished in the reactor or the catalyst can be removed and regenerated off-site. After regeneration, it is necessary to reduce and sulfide the catalyst before it is returned to service. In the absence of permanent poisons such as arsenic or lead on the catalyst, it is possible to regenerate a catalyst charge as many as 10 times and achieve a catalyst life as long as 10 years before replacement is necessary (see CATALYSTS, REGENERATION).

The British Petroleum Cyclar process started up for the first time in 1989 uses a proprietary 1 wt % gallium on ZSM-5 zeolite catalyst to convert liquified petroleum gas, eg, butane and propane, or any mixture of the two, into aromatics and hydrogen in a single step at low pressure at 500°C. The process uses a four-stage moving bed, radial flow reactor with provision for continuous catalyst regeneration. Benzene, xylene, and toluene comprise over 90% of the liquid products; the methane and ethane produced are used as fuel for the process. Over 45 wt % greater hydrogen yield is obtained than with naphtha reforming. This process is an important addition to chemical technology because of the long-term expected oversupply of LPG and the reduced need for butane in gasoline.

Oxidation. Oxidation reactions utilizing supported catalysts usually present extraordinary challenges, because most oxidations are highly exothermic and may generate extremely high localized temperatures that the catalyst surface must survive to have an adequately long service lifetime. In addition, in many cases the desired product is subject to further oxidation, which must be prevented or minimized.

Partial Oxidation of Ethylene to Ethylene Oxide. About 3.3 million metric tons of ethylene oxide were produced worldwide in 1988. Of this, about 70% was converted into ethylene glycol, and the balance went into detergents and other applications. An excellent review of ethylene oxide synthesis has been written (66).

Ethylene oxide (qv) was once produced by the chlorohydrin process, but this process was slowly abandoned starting in 1937 when Union Carbide Corp. developed and commercialized the silver-catalyzed air oxidation of ethylene process patented in 1931 (67). Union Carbide Corp. is still the world's largest ethylene oxide producer, but most other manufacturers license either the Shell or Scientific Design process. Shell has the dominant patent position in ethylene oxide catalysts, which is the result of the development of highly effective methods of silver deposition on alumina (29), and the discovery of the importance of establishing precise parts per million levels of the higher alkali metal elements on the catalyst surface (68). The most recent patents describe the addition of trace amounts of rhenium and various Group (VI) elements (69).

Ethylene oxide is produced in large, multitubular reactors cooled by pressurized boiling liquids, eg, kerosene and water. Up to 100 metric tons of catalyst may be used in a plant. Typical feed stream contains about 30% ethylene, 7–9% oxygen, 5–7% carbon dioxide; the balance is diluent plus 2–5 ppmw of a halogenated moderator. Typical reactor temperatures are in the range 230–300°C. Most producers use newer versions of the Shell cesium-promoted silver on alumina catalyst developed in the mid-1970s.

Catalyst lifetime for contemporary ethylene oxide catalysts is 1–2 years, depending on the severity of service, ie, ethylene oxide production rate and absence of feed poisons, primarily sulfur compounds. A large percentage (>95%) of the silver in spent catalysts can be recovered and recycled; the other components are usually discarded because of their low values.

Three reactions dominate ethylene oxide production:



Equation 1 is referred to as the selective reaction, equation 2 is called the nonselective reaction, and equation 3 is termed the consecutive reaction and is considered to proceed via isomerization of ethylene oxide to acetaldehyde, which undergoes rapid total combustion under the conditions present in the reactor. Only silver has been found to effect the selective partial oxidation of ethylene to ethylene oxide. The maximum selectivity for this reaction is considered to be 85.7%, based on mechanistic considerations. The best catalysts used in ethylene oxide production achieve 80–84% selectivity at commercially useful ethylene–oxygen conversion levels (68,69).

Silver has been supported successfully on both alumina and low silica content silica–alumina, but today's catalysts use only low surface area (<1 m²/g) α-Al₂O₃. Commercial silver catalysts have contained metal loadings in the range 7–30 wt % deposited on the support by a number of methods, including (1) rolling the support in silver oxide followed by calcination; (2) impregnating the support with silver nitrate solution and reducing with hydrogen; (3) impregnating with aqueous silver lactate and heating to decompose the salt; and (4) impregnating with silver carboxylates solubilized with various amines and heating to form the metal. A finer silver dispersion has been claimed by The Dow Chemical Company (70), and a new way to solubilize silver using a C₇ or higher neoacid is described by Scientific Design (71).

Shaped alpha-alumina macroporous pellets and rings with sizes in the range 5–8 mm diameter and length have been the support of choice for the past two decades. The following support properties are important: chemical purity, strength, resistance to attrition, surface area, pore volume, and median pore size. In more recent patent filings, workers in Japan have defined what they believe to be desirable acid–base characteristics of alumina supports (72). Shell researchers in Holland seek to alter acid–base characteristics of alpha-alumina by the addition of tin compounds (73), and The Dow Chemical Company claims that adding barium to the support improves crush strength and abrasion resistance (74). German workers suggest a minimum geometrical support surface area of 600 m²/m³ of reactor volume for optimum performance (75), and a group in Japan describes the use of a saddle shaped support (76).

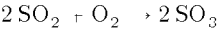
Ethylene oxide catalyst research is expensive and time-consuming because of the need to break in and stabilize the catalyst before reliable data can be collected. Computer controlled tubular microreactors containing as little as 5 g of catalyst can be used for assessment of a catalyst's initial performance and for long-term life studies, but moving basket reactors of the Berty (77) or Carberry (78) type are much better suited to kinetic studies.

Pilot plants utilizing a single-full-sized reactor tube from a commercial plant are generally used to assess the quality and performance of individual catalyst lots and to perform plant or customer ordered process tests. A well-designed pilot unit is capable of simulating the performance of a commercial plant with great accuracy.

n-Butane Oxidation to Maleic Anhydride. In the conventional fluid-bed process, butenes are air-oxidized to maleic anhydride (qv) in 50–60% yield. In a new process developed by DuPont, maleic anhydride yields of 70–75% are achieved by separating the n-butane oxidation from the catalyst oxidation. This is accomplished with the use of a moving-bed reactor in which n-butane [106-97-8] is oxidized by a silica-supported vanadium oxide catalyst that is regenerated in a separate reactor by air oxidation. A special, vanadium–phosphate catalyst was developed for this application using polysilicic acid to generate a porous, attrition-resistant silica shell that gives mechanical strength without sacrificing activity. As part of an integrated process, the maleic anhydride [108-31-6] produced is hydrogenated to tetrahydrofuran in aqueous solution using a proprietary rhenium-promoted palladium catalyst (79).

Catalytic Sulfur Dioxide Oxidation. Sulfuric acid [7664-93-9] is the largest volume chemical manufactured worldwide and is produced by

hydration of sulfur trioxide in packed towers. In virtually all cases, sulfur trioxide [7446-11-9] is obtained by the catalytic oxidation of sulfur dioxide [7446-09-5] with oxygen over a vanadium-based catalyst (80):



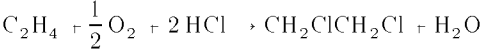
This catalyst is noteworthy in that it represents a good example of a liquid active phase, actually molten at the typical 600°C + process temperatures, supported on a solid support.

The active phase, which is solid at room temperature, is comprised of mixed potassium and sodium vanadates and pyrosulfates, whereas the support is macroporous silica, usually in the form of 6–12 mm diameter rings or pellets. The patent literature describes a number of ways to prepare the catalyst; a typical example contains 7 wt % vanadium pentoxide, 8% potassium added as potassium hydroxide or carbonate, 1% sodium, and 78 wt % silica, added as diatomaceous earth or silica gel, formed into rings, and calcined in the presence of sulfur dioxide or sulfur trioxide to convert a portion of the alkali metal salts into various pyrosulfates (81,82).

Catalyst lifetimes are long in the absence of misoperation and are limited primarily by losses to fines, which are removed by periodic sieving. Excessive operating temperatures can cause degradation of the support and loss of surface area. Accumulation of refractory dusts and chemical poisons, such as compounds of lead and mercury, can result in catalyst deactivation. Usually, much of such contaminants are removed during sieving. The vanadium in these catalysts may be extracted and recycled when economic conditions permit.

Reproducible measurements of absolute activity for sulfur dioxide oxidation catalysts are very difficult to obtain for a number of reasons, including the fact that the reaction is extremely fast. In addition, there are differences in techniques and reporting methods used by the various workers. Pulse microreactors have been used to study quantities of these catalysts as small as 500 mg (83).

Oxychlorination of Ethylene to Dichloroethane. Ethylene (qv) is converted to dichloroethane in very high yield in fixed-bed, multitubular reactors and fluid-bed reactors by reaction with oxygen and hydrogen chloride over potassium-promoted copper(II) chloride supported on high surface area, porous alumina (84):



Oxychlorination catalysts are prepared by impregnation methods, though the solutions are very corrosive and special attention must be paid to the materials of construction. Potassium chloride is used as a catalyst component to increase catalyst life by reducing losses of copper chloride by volatilization. The catalysts used in fixed-bed reactors are typically 5 mm diameter rings or spheres, whereas a 20–100 micrometer powder is used in fluid-bed operations.

Oxychlorination of ethylene to dichloroethane is the first reaction performed in an integrated vinyl chloride plant. In the second stage, dichloroethane is cracked thermally over alumina to give vinyl chloride and hydrogen chloride. The hydrogen chloride produced is recycled back to the oxychlorination reactor.

The oxychlorination reaction is very exothermic and the catalyst is very active, which makes it necessary to mix the catalyst with an inert diluent to avoid overheating in a fixed-bed reactor. A low surface area, spherically- or ring-shaped alumina or chemical porcelain body can be used as a diluent with the ring-shaped catalyst. The density of the inert material should be similar to the catalyst to avoid segregation during loading, and the size should be slightly different to allow separation of the inert material from the spent catalyst.

Polymerization. Supported catalysts are used extensively in olefin polymerization, primarily to manufacture polyethylene and polypropylene. Because propylene can polymerize in a stereoregular manner to produce an isotactic, or crystalline, polymer as well as an atactic, or amorphous, polymer and ethylene cannot, there are large differences in the catalysts used to manufacture polyethylene and polypropylene (see OLEFIN POLYMERS).

Olefin polymerization catalysts are unique in their utilization of supported catalysts in that the catalysts that have been developed are so highly active that the spent catalysts are intentionally left in the polymer where, at the extremely low parts per million concentrations used, they pose no threat to the properties of the polymer or to the well-being of the end user.

Polyethylene. Low pressure polymerization of ethylene produced in the Phillips process utilizes a catalyst comprised of 0.5–1.0 wt % chromium (VI) on silica or silica–alumina with pore diameter in the range 5–20 nanometers. In a typical catalyst preparation, the support in powder form is impregnated with an aqueous solution of a chromium salt and dried, after which it is heated at 500–600°C in fluid-bed-type operation driven with dry air. The activated catalyst is moisture sensitive and usually is stored under dry nitrogen (85).

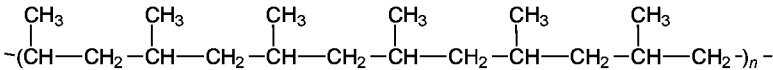
The Phillips-type catalyst can be used in solution polymerization, slurry polymerization, and gas-phase polymerization to produce both high density polyethylene homopolymers and copolymers with olefins such as 1-butene and 1-hexene. The less crystalline copolymers satisfy needs for materials with more suitable properties for certain uses that require greater toughness and flexibility, especially at low temperatures.

Union Carbide Corp. also uses a silica-supported chromium catalyst in their extremely low cost Unipol gas-phase linear low density ethylene copolymer process, which revolutionized the industry when it was introduced in 1977 (86–88). The productivity of this catalyst is 10⁵–10⁶ kg polymer/kg transition metal contained in the catalyst. By 1990, the capacity of Unipol linear low density polyethylene reactors was sufficient to supply 25% of the world's total demand for polyethylene.

In all of the ethylene polymerization processes, the catalyst is sensitive to feed impurities and is poisoned by most polar compounds. Many of the properties of the polymer are determined by polymerization conditions, but catalyst composition and condition are critical determinants as well. Cocatalysts, such as diethylzinc and triethylboron, can be used to alter the molecular-weight distribution of the polymer (89). The same effect can also be had by varying the transition metal in the catalyst; chromium-based catalyst systems produce polyethylenes with intermediate or broad molecular-weight distributions, but titanium catalysts tend to give rather narrow molecular-weight distributions.

Polypropylene. There is an added dimension to the catalytic polymerization of propylene, since in addition to the requirement that the catalyst be sufficiently active to allow minute amounts of catalyst to yield large quantities of polymer, it must also give predominantly polypropylene with high tacticity; that is, a highly ordered molecular structure with high crystallinity. The three structures for polypropylene are the isotactic, syndiotactic, and atactic forms (90) (see OLEFIN POLYMERS, POLYPROPYLENE).

In the propylene polymer the pendent methyl group is attached to an asymmetric carbon atom.



In isotactic polypropylene, all pendent methyl groups are aligned in the same direction, as shown, and this stereoregular polymer configuration is, consequently, highly crystalline and has a relatively high melting point. In syndiotactic polypropylene, the pendent methyl groups alternate on opposite sides of the chain in a regular manner and the polymer is not crystalline but tends to be elastomeric. In atactic polypropylene, the pendent methyl groups are randomly arranged, and the polymer is a sticky semisolid.

The syndiotactic polymer configuration is not obtained in pure form from polymerizations carried out above 20°C and, thus has not been a serious concern to most propylene polymerization catalyst designers. For most commercial applications of polypropylene, a resin with 96+% isotacticity is desired. Carbon-13 nmr can be used to estimate the isotactic fraction in a polypropylene sample. Another common analytical method is to dissolve the sample in boiling xylene and measure the amount of isotactic polymer that precipitates on cooling.

From 1955–1975, the Ziegler-Natta catalyst (91), which is titanium trichloride used in combination with diethylaluminum chloride, was the catalyst system for propylene polymerization. However, its low activity, which is less than 1000 g polymer/g catalyst in most cases, and low selectivity (ca 90% to isotactic polymer) required polypropylene manufacturers to purify the reactor product by washing out spent catalyst residues and removing unwanted atactic polymer by solvent extraction. These operations added significantly to the cost of pre-1980 polypropylene.

Supported Catalysts for Propylene Polymerization. Although magnesium halide supported titanium catalysts for propylene

polymerization were studied as early as the 1950s, the first such catalyst available commercially was the FT-1 catalyst announced in 1976, a product of an intensive joint research effort by Montedison in Italy and Mitsui in Japan. This catalyst was produced by the intensive ballmilling of anhydrous magnesium chloride with an electron donor, usually ethyl benzoate [73-89-0], to obtain crystallites of the $\text{MgCl}_2\text{-C}_2\text{H}_5\text{OOC C}_6\text{H}_5$ complex as small as 5–6 nanometers in diameter, which were used as the support on which titanium tetrachloride was deposited by additional ballmilling (28).

Triethylaluminum, complexed with another electron donor, typically ethyl *p*-anisate [94-30-4], was used as cocatalyst with the FT-1 catalyst and acted to reduce and stabilize the active titanium-containing catalytic site. The early versions of the FT-1 catalyst required extremely high molar ratios (>400 : 1) of aluminum to titanium to obtain satisfactory activity and selectivity to isotactic polymer. This resulted in excessively high aluminum residues in the polymer. Later versions of the FT-1 catalyst attained much higher activity.

With the use of the most recent version of the FT-1-type catalyst in their Spheripol process, Himont claims that high activity, high selectivity, full molecular-weight control and full morphology control are provided in bulk propylene polymerization (92). In addition, propylene can be polymerized sequentially with other monomers in Himont's Catalloy process to form polymer alloys. These products are claimed to have properties that allow them to compete with poly(vinyl chloride), and polystyrene. In bulk homopolymerization, the porous, spherical magnesium chloride supported titanium catalyst produces large, spherical, porous, free-flowing polypropylene particles directly from the reactor, which makes it unnecessary to form the polymer into nibs for shipping and handling. Color additives and stabilizers, which are added to conventional polypropylene powder during the production of nibs, can be blended directly into the solid Spheripol polymer because of its highly porous texture.

Probably the highest activity, highest selectivity magnesium chloride supported titanium catalyst presently available is Shell's super high activity catalyst (SHAC). Unlike the Montedison-Mitsui ballmilling approach to catalyst manufacture used in FT-1 manufacture, the Shell version relies on forming the support and catalyst in a proprietary chemical method of preparation (27) that avoids the damaging effects of contact of the procatalyst with moisture. Like other supported catalysts, the Shell catalyst is used with an alkylaluminum cocatalyst and electron-donor system. Early versions of SHAC were used in bulk polymerization processes to produce polypropylene with 95 + % isotacticity and <100 ppmw catalyst residues. The latest versions have been successfully adapted for use in the Union Carbide - Shell Unipol gas-phase polypropylene process, which, because of its simplicity, requires lower capital investment and operating costs than other propylene polymerization processes.

New Developments in Supported Catalysts

Some areas of current interest include methane coupling to C₂ + hydrocarbons, oxidation of methane to useful products, conversion of propane to acrylonitrile, and synthesis gas to oxygenates. A largely unexplored area with vast potential is the supporting of enzymes to effect and control biologically important reactions. New ways to support catalytically active materials are being considered, such as with the use of an immiscible liquid to support a catalyst in solution. The rational application of purely theoretical considerations to catalyst design will be increasingly important.

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REGENERATION

Fluid catalytic cracking units,
Noble metal and base metal catalysts,

FLUID CATALYTIC CRACKING UNITS

The process of fluid catalytic cracking (FCC) is the central process in a modern, gasoline-oriented refinery. In U.S. refineries, the amount of feed processed by fluid catalytic cracking units (FCCU) is equivalent to 35% of the total crude oil processed in the United States (1). As of January 1991, installed FCCU capacity in the United States was $8.6 \times 10^6 \text{ m}^3 \text{ d}$ ($5.4 \times 10^6 \text{ barrels d}$).

The popularity of the catalytic cracker stems from its ability to produce large quantities of high octane gasoline and other valuable light products and to use a wide range of refinery process streams as feed materials. The FCCU feeds include high molecular-weight vacuum gas oils (VGO), which are traditional feeds; atmospheric and vacuum residues; coker gas oils; gas oils from other thermal and hydrocracking operations; lube oil extracts; and deasphalted oils. In a modern U.S. gasoline refinery, the FCCU typically produces about 35% of the total refinery gasoline pool (2).

Although the FCCU has long been an important refinery processing tool in the United States, refinery gasoline demands outside the United States have been satisfied largely from the gasoline naturally present in crude oil (3). This situation is changing, and the need for catalytic cracking is now growing steadily everywhere. Worldwide, excluding North America, Eastern Europe, and mainland China, installed FCCU capacity increased nearly 60% in the 10-year period from 1981 to 1991, and in 1991 stood at $7.3 \times 10^6 \text{ m}^3 \text{ d}$ ($4.6 \times 10^6 \text{ barrels d}$) (4,5).

The FCC process is highly complex but self-contained. A typical unit of mid-1980s design is shown in Figure 1 (6). In the reactor section, hydrocarbon feed is combined with hot fluidizable cracking catalyst at the base of the riser reactor. Catalyst and hydrocarbon vapors pass up the riser in a dilute-phase, plug-type flow and discharge into the reactor vessel where catalyst and hydrocarbon vapors are separated. When in contact with the catalyst, the hydrocarbon feed cracks to form gasoline, middle distillates, liquefied petroleum gas (LPG), and fuel gas. Coke, which is also formed, deposits on the catalyst surface and greatly reduces the catalyst activity. To restore its activity, the catalyst passes into the regenerator section where the coke is burned off. The heat released from coke burning is completely used to provide the heat requirements on the reactor side: to vaporize the feed, to compensate for the endothermic heat of cracking, to bring the reactor to the desired reactor temperature, and to compensate for heat losses to the atmosphere.

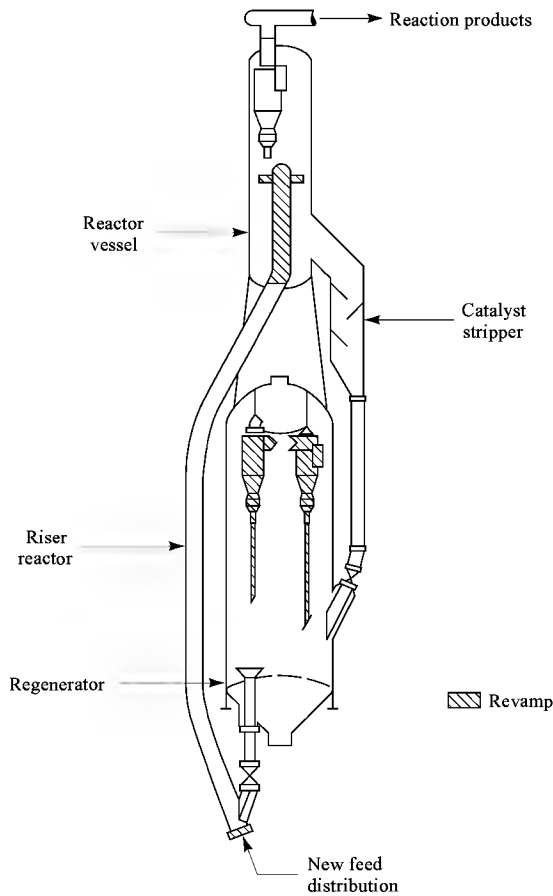


Fig. 1. UOP stacked FCC unit revamped to riser cracking (6).

Thus the FCCU always operates in complete heat balance at any desired hydrocarbon feed rate and reactor temperature; this heat balance is achieved in units such as the one shown in Figure 1 by varying the catalyst circulation rate. Catalyst flow is controlled by a slide valve located in the catalyst transfer line from the regenerator to the reactor and in the catalyst return line from the reactor to the regenerator. In some older style units of the Exxon Model IV-type, where catalyst flow is controlled by pressure balance between the reactor and regenerator, the heat-balance control is more often achieved by changing the temperature of the hydrocarbon feed entering the riser.

Prior to entering the regenerator, the spent catalyst from the reactor passes through a steam stripper where the hydrocarbon vapors that are entrained by the flowing catalyst particles are displaced by steam. The steam also acts to desorb some of the lighter hydrocarbons that are adsorbed during the reaction step. These stripped materials, which represent valuable reaction products, are carried back into the reactor by the upflowing steam from the stripper and go to the product-recovery section with the other reaction products. The removal of these materials from the catalyst stream flowing to the regenerator also reduces the amount of burnable hydrocarbon going to the regenerator, which helps to decrease the regenerator temperature.

FCCU Heat Balance

Because of the thermal coupling of reactor and regenerator, any change on the reactor side creates a rapid change on the regenerator side, which, in turn, influences the reactor side, and vice versa. This dynamic interaction rapidly comes to equilibrium, and the catalytic cracker adjusts to a new steady-state,

heat-balanced condition. The first law of FCCU catalytic cracking is that the FCCU will always adjust itself to stay in heat balance (7). If an FCCU is not in heat balance, it is out of control. The operating characteristics of an FCCU regenerator are thus dictated by the constraints of the heat balance (Fig. 2).

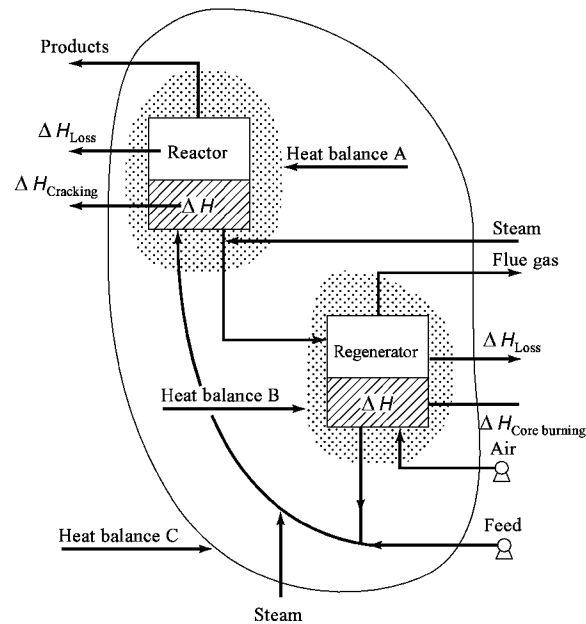


Fig. 2. Heat balance of the FCCU. Heat balance around the reactor A, heat balance around the regenerator B, and the overall heat balance around the entire catalytic cracker C must be considered.

Considering the overall balance, the burning of coke in the regenerator provides all of the energy required to raise the temperature of the reactor hydrocarbon feed and products to the reactor vessel temperature; raise the temperature of the combustion air from the temperature of the air blower discharge to the temperature of the regenerator flue gas; provide the endothermic heat of reaction; provide the heat that is removed from the system, including natural heat loss from the reactor and regenerator to the atmosphere as well as intentional heat removal from catalyst coolers.

$$\Delta H_{\text{Coke combustion}} - \Delta H_{\text{Products-feed}} + \Delta H_{\text{Air}} + \Delta H_{\text{Cracking}} + \Delta H_{\text{Loss}} \tag{1}$$

Thus the amount of heat that must be produced by burning coke in the regenerator is set by the heat balance requirements and not directly set by the coke-making tendencies of the catalyst used in the catalytic cracker or by the coking tendencies of the feed. Indirectly, these tendencies may cause the cracker operator to change some of the heat-balance elements, such as the amount of heat removed by a catalyst cooler or the amount put into the system with the feed, which would then change the amount of heat needed from coke burning.

If FCCU operations are not changed to accommodate changes in feed or catalyst quality, then the amount of heat required to satisfy the heat balance essentially does not change. Thus the amount of coke burned in the regenerator expressed as a percent of feed does not change. The consistency of the coke yield, arising from its dependence on the FCCU heat balance, has been classified as the second law of catalytic cracking (7).

Coke Formation

The coke burned in an FCCU regenerator is a poorly defined, hydrocarbonaceous material that has either not been desorbed from the catalyst surface or has not been purged from between catalyst particles during the passage of the catalyst through the steam stripper. This coke originates from four different sources (8): (1) catalytic coke is produced directly from the acid catalyzed cracking reaction; (2) contaminant coke arises from the dehydrogenation activity of contaminating metals (principally nickel and vanadium) in the feed to the FCCU; (3) additive coke is directly related to the high boiling, refractory components in the feed to the FCCU. This coke correlates with the basic nitrogen and molecular weight of the feed (9) and with the carbon residue content of the feed (8); and (4) cat-to-oil coke is related to the catalyst circulation rate and derives from the hydrocarbons leaving the stripper. These hydrocarbons are potentially strippable but because of incomplete stripping are entrained by the flowing catalyst into the regenerator. FCCU coke distributions for operations with zeolitic catalysts are given in Table 1 (8,10).

Table 1. FCCU Coke Distributions, % of Total Coke

Feed type	Catalytic	Contaminant	Additive	Cat oil
VGO	65	15	5	15
resid	29	29	35	7

^a Ref. 8 and 10.

The amount of catalytic coke that is formed depends on the type of catalyst used in the FCCU, the coking tendency of the feed, the degree of conversion of the feed, and the length of time the catalyst is exposed to the feed (eq. 2) (11).

$$\text{coke on catalyst} = kt^{1/2} \tag{2}$$

Coke deposition is essentially independent of space velocity. These observations, which were developed from the study of amorphous catalysts during the early days of catalytic cracking (11), still characterize the coking of modern day zeolite FCC catalysts over a wide range of hydrogen-transfer (H-transfer) capabilities.

Coke on the catalyst is often referred to as delta coke (ΔC), the coke content of the spent catalyst minus the coke content of the regenerated catalyst. Delta coke directly influences the regenerator temperature and controls the catalyst circulation rate in the FCCU, thereby controlling the ratio of catalyst: hydrocarbon feed (cat-to-oil ratio, or C/O). The coke yield as a fraction of feed C_F is related to delta coke through the C/O ratio as:

$$C_F = \left(\frac{C}{O}\right) \Delta C \tag{3}$$

The catalytic conversion of gas oil is well approximated by a second-order reaction where sv = space velocity (12).

$$\text{conversion}_{\text{2ndorder}} = \frac{\text{conv}}{100} = \frac{k}{sv}$$

4

Space velocity is related to the C/O ratio through the catalyst residence time as:

$$\frac{C}{O} = \frac{1}{(sv) t}$$

5

Combining equations 3, 4, and 5 gives:

$$C_F = \frac{\Delta C}{kt} \text{conv}_{\text{2ndorder}}$$

6

Equation 6 relates the catalytic coke yield (as a fraction of the feed) to the delta coke, to the conversion, and to the catalyst residence time.

It has been shown that coke yield as a fraction of feed does give a linear relationship with second-order conversion (13) indicating a positive coke yield at zero conversion. This coke yield at zero conversion is the additive coke contribution to the total coke yield and is related to feed properties, particularly Conradson carbon content. The amount of this additive coke is significantly less than the Conradson carbon value of the feed (14), probably in the range of 50% of the Conradson carbon.

Catalytic coke is also a function of the type of feed being processed. The more aromatic the feed, the higher the coke (on feed) yield at a given conversion (13). The type of cracking catalyst also influences the coke yield. Increasing the H-transfer characteristics of a Y-type zeolite, by increasing the amount of rare earth exchanged on the zeolite, results in an increase in the catalytic coke yield (15). Modern catalysts for FCC applications frequently contain an active zeolite component plus an active, nonzeolitic component, typically a catalytically active alumina in the so-called matrix portion of the catalyst surrounding the zeolite. Increasing matrix activity typically increases coke yield at constant conversion (16).

Contaminant coke can vary substantially because of large variations in the metals content of the feed being processed and from variations in the manner that cracking catalysts respond to these metals. Nickel is considered the most active dehydrogenation agent and hence the most troublesome of the contaminant metals. Copper is equally active as a dehydrogenation catalyst, but the amount of copper present is usually too small to have an effect. Typically, copper in the feed to the FCCU is only 2–5% of the nickel content. Vanadium is a less active dehydrogenation agent than nickel, about one-fourth as effective as nickel (8). The metals content of the equilibrium catalyst in the FCCU is frequently referred to as the equivalent nickel content, which is defined as:

$$\text{equivalent nickel} = \text{Ni} + \frac{\text{V}}{4}$$

7

The equivalent nickel content of the feed to the FCCU can vary from <0.05 ppm for a well-hydrotreated VGO to >20 ppm for a feed containing a high resid content. The nickel and vanadium deposit essentially quantitatively on the cracking catalyst and, depending on catalyst addition rates to the FCCU, result in total metals concentrations on the equilibrium catalyst from 100 to 10,000 ppm.

At high metals levels, the coking characteristics of a cracking catalyst can be greatly increased; that is, the ratio of contaminant coke to catalytic coke can be quite high. The effect of the contaminant metals on the coke response is affected not only by the level of metals but also by the type of catalyst and the use of a metals passivator. Catalysts, which contain effective metals traps to inhibit the contaminant effects, do produce much less contaminant coke than catalyst without metal traps.

Additive inhibitors have been developed to reduce the contaminant coke produced through nickel-catalyzed reactions. These inhibitors are injected into the feed stream going to the catalytic cracker. The additive forms a nickel complex that deposits the nickel on the catalyst in a less catalytically active state. The first such additive was an antimony compound developed and first used in 1976 by Phillips Petroleum. The use of the antimony additive reportedly reduced coke yields by 15% in a commercial trial (17).

During the 1980s, antimony was widely used in FCCUs that had a problem with contaminant metals. In the late 1980s, other additives were introduced to combat the contaminant metals, eg, Chevron introduced a bismuth-based additive, which is claimed to provide performance similar to antimony (18). Also in the late 1980s, cracking catalysts were developed with metals traps that appear to be so effective in containing the adverse effects of contaminant metals that additive-type inhibitors are no longer needed (19).

Coke Burning

The burning of coke in the regenerator provides the heat to satisfy the FCCU heat balance requirements as shown in equation 1. The heat released from the burning of coke comes from the reaction of carbon and hydrogen to form carbon monoxide, carbon dioxide, and water. The heat generated from burning coke thus depends on the hydrogen content of the coke and the relative amounts of carbon that burn to CO and CO₂, respectively.

Reaction	ΔH_{comb} , kJ/kg of C or H ₂
H ₂ + $\frac{1}{2}$ O ₂ → H ₂ O (g)	121,000
C + O ₂ → CO ₂ (g)	32,700
C + $\frac{1}{2}$ O ₂ → CO (g)	9,200

The impact that variations in coke content and burning conditions can have on the overall heat of coke combustion is shown in Table 2. Because the heat balance dictates the amount of heat that is required from burning coke, the heat of combustion then determines the amount of coke that must be burned.

$$\text{coke required, kg/h} = \frac{\text{combustion heat required, kJ/h}}{\text{specific heat of combustion, kJ/g}}$$

8

Table 2. Specific Heat of Coke Combustion

H ₂ , wt % in coke	Flue gas, CO ₂ /CO	Specific heat kJ/kg coke ^a
12	∞	43,300
7	∞	38,900
7	1.0	28,000

^a To convert kJ to kcal, divide by 4.184.

Decreasing the specific heat of combustion increases the amount of the coke that must be burned; the coke component that increases is essentially the cat-to-oil coke, which is increased by increasing the catalyst circulation rate. Cat-to-oil coke can be expressed as (20):

$$\text{coke} = f \left[(\text{catalyst circulation rate})^{0.65} \right]$$

(9)

Thus decreasing the specific heat of combustion results in an increase in catalyst circulation rate. Because of this relationship to coke yield (eq. 9), the increase in the catalyst circulation rate results in a decrease in regenerator temperature.

The hydrogen content of the coke can vary considerably, depending on the efficiency of the stripping operation to remove the lighter hydrocarbons from the catalyst flowing into the regenerator. Hydrogen content in the coke can vary from 4–5 wt % for a highly efficient stripping operation up to 13–15 wt % for poor stripping. The hydrogen content in a well run FCCU is in the range of 6–8 wt %.

The oxidation of carbon on the catalyst surface (coke burning) is believed to proceed through the formation of solid surface oxides, which decompose to give both CO and CO₂ as primary products (21). In an early study on the burning of graphite, it was shown that the CO₂/CO ratio is constant throughout the burning cycle, independent of oxygen partial pressure, and dependent only on the combustion temperature (22). The burning of carbonaceous deposits from porous oxides produced CO₂/CO ratios at the burning site in exact agreement with the ratios of the earlier study (22) over the temperature range 450–600°C (23). Diffusion effects in the pores of large catalyst particles influence the CO₂/CO ratio in the bulk vapor phase (23). However, for particle sizes typical of FCC operations (60–70 μm average particle size), diffusion is not a factor, and thus particle size would not influence the CO₂/CO ratio. Consequently, this molar ratio remains relatively constant at a value of about 1.0 for many regenerators operating in the region below 700°C and in the absence of a CO combustion promoter.

The rate of coke burning for coke deposited on a zeolite-containing catalyst has been reported to be first order with respect both to coke concentration *c_C* and oxygen partial pressure (23):

$$\frac{dc_C}{dt} = kc_C P_{O_2}$$

(10)

This equation is in agreement with coke-burning studies on amorphous silica-alumina catalysts (24,25). Other investigators have found that carbon burning was second order (26) or mixed order (27) with respect to carbon. It has been argued that coke burning follows first-order kinetics but only after an initial period of several minutes, when burning is not first order with carbon content (28). The data in Figure 3 on coked FCC catalyst of the H-Y type agree with this argument.

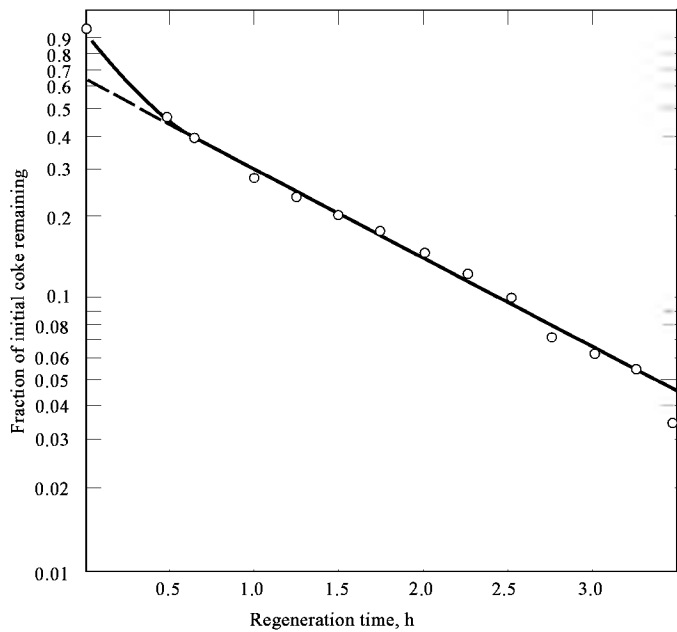


Fig. 3. Burning at 500°C in flowing air of coke from H-Y FCC catalyst.

The activation energy for burning from a coked zeolite has been reported as 109 kJ/mol (29) and 125 kJ/mol (30 kcal/mol) has been found for coke burning from a H-Y FCC catalyst. Activation energies of 167 kJ/mol (40 kcal/mol) (24) and 159 kJ/mol (25) have been reported for the burning of carbon from a coked amorphous silica–alumina catalyst.

The coke-burning rate in the regenerator is thus a function of the oxygen partial pressure, the carbon content on the catalyst leaving the reactor, the temperature in the regenerator, and the residence time in the regenerator. The last three variables are all coupled together through the FCCU heat-balance requirements. For example, an increase in regenerator temperature normally results in a decrease in catalyst circulation rate to maintain a constant temperature on the reactor side. The decrease in catalyst circulation rate increases the residence time in the regenerator and is accompanied by a change in the carbon content of the catalyst coming into the regenerator. A typical interrelationship between the O₂ content in the regenerator flue gas, the regenerator temperature, and the carbon content of the regenerated catalyst (CRC) is shown in Figure 4. At a constant flue gas O₂ content, a decrease in regenerator temperature of 20°C results in a CRC increase of 0.15–0.20 wt %.

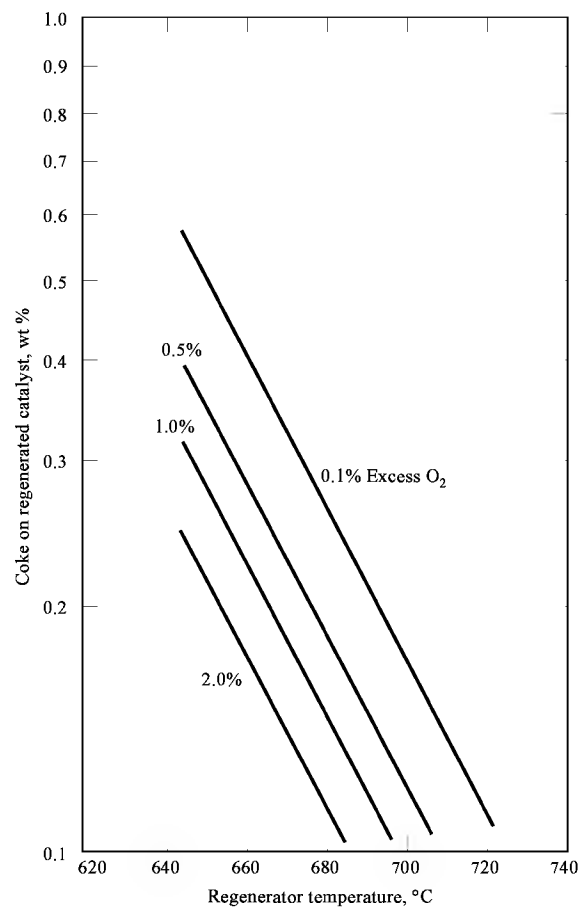


Fig. 4. Coke on regenerated catalyst (CRC) versus regenerator temperature at varying O₂ content (30).

The hydrocarbon feed rate to the reactor also affects the burning kinetics in the regenerator. Increasing the reactor feed rate increases the coke production rate, which in turn requires that the air rate to the regenerator increase. Because the regenerator bed level is generally held constant, the air residence time in the dense phase decreases. This decrease increases the O₂ content in the dilute phase and increases afterburn (Fig. 5).

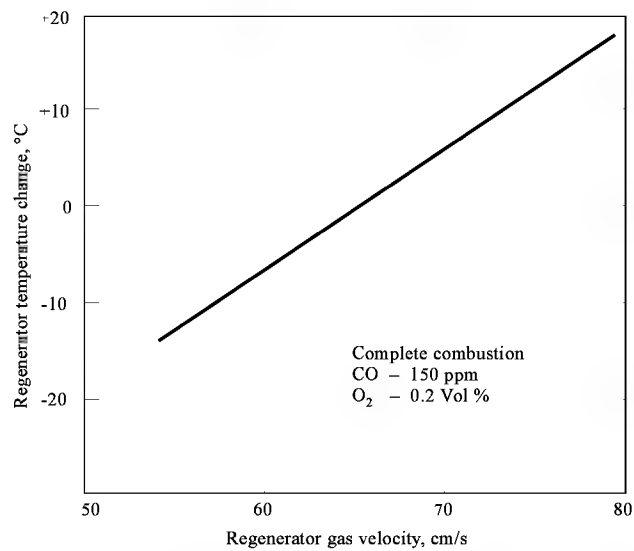


Fig. 5. Effect of gas residence time on afterburning. The temperature change ΔT is the difference in temperature between flue and dense phase (30).

The coke-burning rates on silica–alumina catalysts have been found to increase several orders of magnitude when transition-metal oxides are present (25). The addition of 0.15 wt % chromium (as Cr₂O₃) to a silica–alumina catalyst produces a nearly fivefold increase in carbon-burning rate. The cation exchanged into a zeolite-containing catalyst affects the burning rate (29). A zeolite exchanged with copper was found to have a burning-rate constant that was 18 times greater than a zeolite exchanged with chromium.

The hydrogen contained in coke burns at a higher rate than carbon. Hydrogen-burning rates are four to five times greater than carbon-burning rates. (24,26)

CO Combustion. The combustion products leaving the coke-burning site consist of both CO₂ and CO, typically at a CO₂ : CO mole ratio of 1.0. The CO formed can then be further oxidized. When a CO combustion promoter is present, the reaction of CO and O₂ to form CO₂ occurs readily in the regenerator dense phase. In the absence of such a promoter, the oxidation of CO occurs slowly in the dense phase below 700°C. This reaction occurs much more rapidly in the regenerator dilute (vapor) phase where it is believed to be catalyzed by the combined presence of fine, decoked metals containing catalyst particles and water vapor (31).

The oxidation of CO to CO₂ releases twice as much heat as does the burning of C to CO. The large heat release coupled with the relatively small amount of mass in the dilute phase produces a large ΔT between the dilute and dense phases in the regenerator. For FCC operations in which a CO combustion promoter is not used, the dilute-phase temperature is frequently 15–40°C higher than the dense phase. In such operations, the control of the regenerator temperature is frequently achieved by adjusting the air rate to the regenerator to maintain an acceptable dilute–dense ΔT . With a substantial

excess of O₂ in the regenerator flue gas (3–4%), complete CO combustion can be achieved without a CO combustion promoter if dense-phase temperatures above 720°C are maintained.

Promoted CO Combustion. In the early 1970s, researchers at Mobil discovered that certain Group (VIII) metals, particularly platinum, can be incorporated into an FCC catalyst system at low concentrations (1–3 wt ppm) to catalyze the combustion of CO to CO₂ effectively (32,33). Of even greater importance was their discovery that at this low incorporation, the Group (VIII) metals did not catalyze undesirable dehydrogenation reactions during the cracking reaction. The cracking-selectivity characteristics achieved by the cracking catalyst in use in the FCCU are thus not altered when such a CO combustion promoter is added to the catalyst inventory.

The use of 1–2 ppm platinum in FCCU circulating catalyst inventories is now widely practiced throughout the world to catalyze the combustion of CO to CO₂ in the FCCU regenerator. The promoter is added to the FCC catalyst inventory either as an integral part of the fresh FCC catalyst, where it is included in the fresh catalyst at 1–2 wt ppm, or as a separate additive. The additive, which typically contains 500–1000 wt ppm of platinum, is added to the FCCU by a small metering system that is independent of the fresh cracking-catalyst addition system. In the United States, the separate additive approach is generally used; in Europe, the additive is most commonly incorporated with the fresh cracking catalyst.

Through the use of a combustion promoter, CO combustion occurs readily in the dense phase at temperatures well below 700°C, eg, one report was at 650°C in a commercial FCCU operation (34).

Promoted combustion has a number of important benefits. First, the afterburn problem, ie, burning in the dilute phase, is greatly reduced. By consuming CO in the dense phase, the potential heat release from burning in the dilute phase is significantly decreased. A commercial example of a 50°C reduction in regenerator afterburn by using a CO combustion promoter is as follows (35):

	Without promoter	With promoter
typical flue gas temperature, °C	699	660
typical dense-phase temperature, °C	663	674
afterburn ΔT, °C	+36	14

The increased flexibility of FCCU operations resulting from using a CO combustion promoter is an even greater advantage. When using a promoter, the air rate to the regenerator can be varied to achieve any degree of CO combustion that is desired. By this mechanism, heat can readily be added to or removed from the regenerator to produce changes in regenerator temperature, catalyst circulation rate, coke yield, and reactor feed conversion. An example of how variations in the degree of CO combustion can effect the performance of an FCCU is seen in Figure 6 (30).

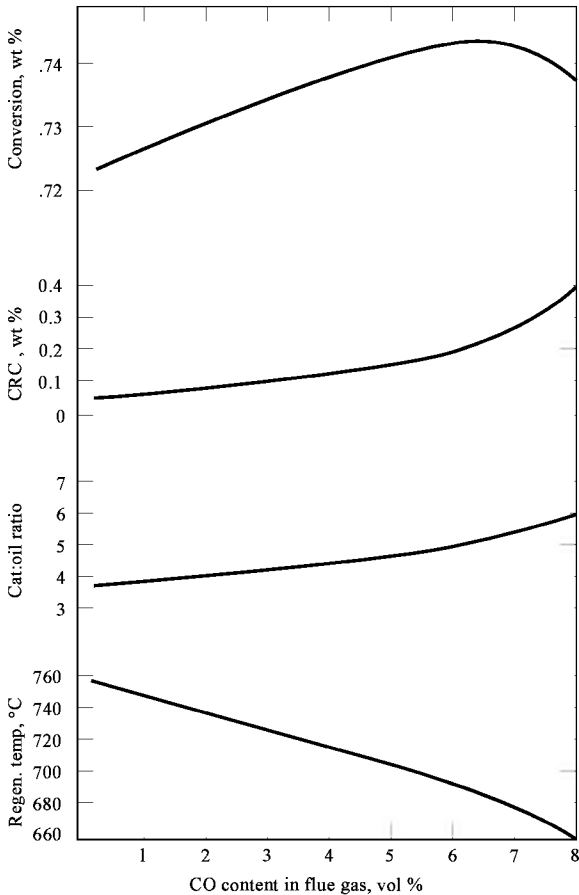


Fig. 6. Typical FCCU interdependency curves (30).

In actual practice, the regenerator temperature is normally controlled at the maximum temperature allowed by the regenerator metallurgy. Variations in feed quality in the FCCU can result in significant regenerator temperature excursions if the degree of CO combustion is unchanged (constant heat of combustion). With a CO combustion promoter present, the degree of CO combustion can be varied to hold the regenerator temperature constant at the desired maximum value even though significant changes in feed quality have occurred. This flexibility is achieved mainly through regenerator air rate control. To a lesser degree, additional flexibility is achieved by controlling the addition rate of fresh CO combustion catalyst to the catalytic cracker. When a CO combustion promoter is used, changes in the air rate affect the amount of CO converted to CO₂ both in the dilute and in the dense phase. Changing the amount of CO burned in turn affects both the dense- and dilute-phase temperatures. Increasing the amount of excess O₂ in the regenerator causes an increase in CO burning in the regenerator dense phase as indicated by an increase in dense-phase temperature. Additional burning in the dilute phase also occurs, causing an increase in ΔT (afterburning) between dense and dilute phases. As a typical example, a decrease in CO content in the regenerator flue gas from 5 to 3 vol % would result in a dilute-phase temperature increase of 31°C, a dense-phase temperature increase of 16°C, and an increase in dilute-dense ΔT of 15°C.

The amount of promoter used can also be a variable in influencing the degree of CO combustion. A promoted catalyst system can be classified as fully or partially promoted. A partially promoted system is one in which an increase in promoter content results in a decrease in the dilute-dense ΔT.

Conversely, a fully promoted system sees no effect on afterburn ΔT when the promoter level is changed. An increase in the promoter content increases the proportion of CO that is burned in the regenerator dense phase. A typical response of afterburn ΔT to promoter change is shown in Figure 7 (7). The change in dilute-dense ΔT is mainly because of changes in the dilute-phase temperature. Changes in promoter concentration have only a small effect on dense-phase temperature but greatly affect dilute-phase temperatures.

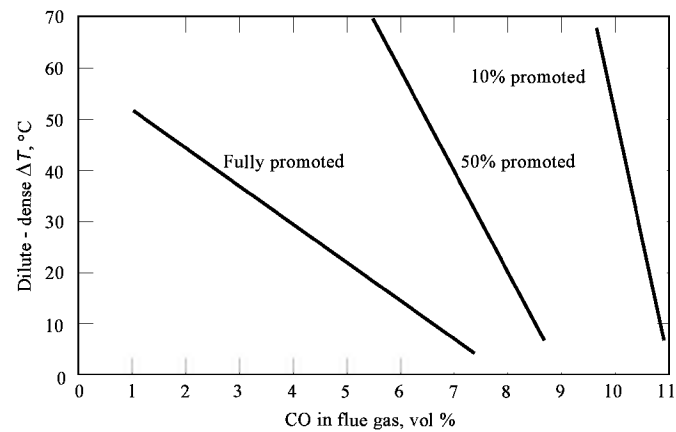


Fig. 7. Effect of promoter concentration on regenerator dilute-dense ΔT (7).

The carbon-burning reaction competes with the coke-burning reaction for the available O_2 in the regenerator. When the O_2 level is low, the amount of promoter present can influence the degree that carbon is burned from the catalyst. In such situations, a high level of promoter enhances the combustion of CO and retards coke burning. A fully promoted catalyst with essentially no excess O_2 in the regenerator equilibrates at a coke content on the regenerated catalyst (CRC) of about 0.1 wt % higher than does a partially promoted system at the same degree of CO combustion (30).

Environmental Aspects

The FCCU regenerator is one of the principal sources of air pollutants from a refinery. A typical 150,000 barrel per day (23,850 m³ d), modern U.S. refinery with a 50,000 bpd FCCU processing a low sulfur, low metals content VGO feed and operating in complete CO combustion typically emits the following into the atmosphere from the FCCU regenerator flue gas stack: fine catalyst particles, 2–3 t d; sulfur oxides, 3–4 t d; nitrogen oxides, 0.5 t d; and CO, 1.5–2 t d. Much research has been done in the past and is ongoing to develop technologies to reduce these emissions.

Catalyst Emissions. High velocity air passing up through the regenerator bed at velocities typically around 1 m s carries large quantities of catalyst into the vapor space above the catalyst bed. To contain these catalyst particles within the regenerator vessel, a highly efficient, generally two-stage cyclone system is installed inside the regenerator. The flue gas and the entrained catalyst particles pass through the cyclone system before exiting from the regenerator. With a two-stage cyclone system, 99.995% or more of the catalyst particles are typically returned by the cyclones back into the regenerator. The particles that are not retained and that leave with the exiting flue gas are small, typically 20 μm average particle size. These particles generally represent fines that have been produced as a result of catalyst attrition.

To reduce catalyst losses even further, additional separation equipment external to the regenerator can be installed. Such equipment includes third-stage cyclones, electrostatic precipitators, and more recently the Shell multitube separator, which is licensed by the Shell Oil Co., UOP, and the M. W. Kellogg Co. The Shell separator removes an additional 70–80% of the catalyst fines leaving the first two cyclones. Such a third-stage separator essentially removes from the flue gas stream all particles greater than 10 μm (36).

Much effort has been made by catalyst manufacturers to improve catalyst attrition resistance and thus reduce the formation of fines (see CATALYSTS, SUPPORTED). In the 10-year period from 1980 to 1990, most catalyst manufacturers improved the attrition resistance of their catalyst by a factor of at least 3–4. This improvement was achieved even though the catalyst zeolite content during this period was continually increasing, a factor that makes achieving catalyst hardness more difficult. As an example of the type of attrition improvement that has been achieved, the catalyst attrition index, which is directly related to catalyst loss rate in a laboratory attrition test, decreased from 1.0 to 0.35 for one constant catalyst grade during 1989–1990 (37).

SO_x Emissions. The amount of SO_x, which refers to the combination of SO₂ and SO₃, emitted from an FCCU regenerator depends on the type of FCC feed (aromatic, paraffinic, hydrotreated), the amount of (organic) sulfur in the feed, and the conversion level. Depending on these factors, 3–12% (typically 5%) of the feed sulfur deposits with the coke on the circulating catalyst (38). This sulfur in the coke is oxidized to SO_x in the regenerator, generally in a mixture of about 90% SO₂ and 10% SO₃ (39). The following general rule of thumb may be used for estimating the regenerator flue SO_x content in parts per million (38):

straight-run feeds: SO_x = 800–1100 × feed sulfur (in wt%)

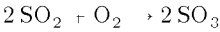
hydrotreated feeds: SO_x = 2050–2800 × feed sulfur (in wt%)

Three possible routes are available to the refiner for the reduction of SO_x emissions from the regenerator: FCC feedstock hydrodesulfurization; flue gas scrubbing; and use of a SO_x removal catalyst. Mild hydrotreating at 3.4–5.5 MPa (500–800 psig H₂ partial pressure) with a modern cobalt–molybdenum catalyst can reduce the sulfur content of the FCC feed by 90% (40). However, hydrotreating increases the fraction of thiophenes in the remaining feed sulfur, and thus a higher fraction of the feed sulfur is retained in the coke (41). Nevertheless, hydrotreating the FCC feed substantially reduces SO_x in the regenerator flue gas. In the case of the 90% feed sulfur reduction, a 70–80% reduction in flue gas SO_x content is achieved.

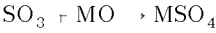
More severe hydrotreating, such as mild hydrocracking at an H₂ partial pressure of >6.9 MPa (1000 psig) and temperature of >400°C, can still further reduce sulfur content in the FCC feed. Mild hydrocracking of a 25° API VGO reduced the sulfur content of the FCC feed 98%, from 1.7 wt % to 0.03 wt % (40). This reduction can be expected to lower the SO_x content in the FCCU regenerator flue gas by about 90%.

Scrubbing the regenerator flue gas is an effective method for removing not only SO_x but also catalyst particulate emissions. In the Exxon wet gas scrubbing system, licensed by the Exxon Research and Engineering Co. and UOP, a recirculating caustic solution is contacted concurrently with the flue gas in a venturitype scrubber. Units of this type have been in use since 1974. Commercial wet gas scrubbers have demonstrated 95% removal of SO₂ and 85% removal of particulate solids from flue gas streams in the FCCU regenerator (42). In 1989, the U.S. Environmental Protection Agency (EPA) set SO_x emissions standards for new FCCUs. In setting these standards, the EPA used data from the Exxon wet gas scrubbing system to represent best demonstrated technology (42).

Currently, the most frequently used technology for SO_x reduction in the flue gas is a SO_x adsorbing additive. With such an additive, the following steps occur:*Oxidation of SO₂ to SO₃ in the regenerator:*



Adsorption of SO₃ in the regenerator by the additive where MO = metaloxide:



Reduction of the metal sulfate in the reactor:



Release of H₂S and regeneration of the metal oxide adsorbent in the stripper:



The H₂S comes out with the reactor products, goes through the product-recovery system of the FCCU, and eventually goes to a Claus plant for sulfur recovery. The metal oxide adsorbent recirculates with the spent cracking catalyst back to the regenerator for the next SO_x adsorption cycle.

A solid solution of a pure magnesium aluminate spinel (MgAl₂O₄) with MgO is an effective metal oxide adsorbent (43). Such a solid solution (Mg₂AlO₅) does not destroy the spinel framework; the MgO adsorbs SO₃ and the adsorption activity of the dispersed MgO in the spinel is much greater than that of pure MgO itself (43).

Cerium is effective in oxidizing SO₂ to SO₃. Consequently, a cerium-impregnated Mg₂Al₂O₅ actively converts the SO₂ to SO₃, which is then strongly adsorbed by the dispersed MgO as MgSO₄. A completely cyclic SO_x removal catalyst contains, in addition to the above component, a fourth metal component such as vanadium to catalyze the conversion of MgSO₄ to MgO (44).

Multifunctional SO_x removal catalyst systems have been in commercial use since 1985 in the United States. Such systems have successfully reduced SO_x emissions in the FCCU regenerator by 50% when the regenerator is operating in the complete CO combustion mode (45). Modern-day additives can achieve a 50% SO_x reduction with only 1S–2% of the additive in the circulating inventory, an amount small enough not to interfere with the cracking characteristics of the bulk FCC catalyst (45).

Because O₂ is necessary to convert SO₂ to SO₃, decreasing O₂ in the regenerator has been found to reduce the effectiveness of the SO_x removal additive. The SO_x additives used in regenerators operating in a partial CO combustion mode, where excess O₂ is frequently limited to <0.2 vol % in the flue gas, are less successful in reducing SO_x. In such cases, SO_x removal is typically 20–30% less than for a full CO combustion (1 + % excess O₂) case (45).

Nitrogen Oxide Emissions. Nitrogen oxide (NO_x) emissions from an FCCU regenerator are much less, typically 100 ppm, than SO_x emissions, and consequently much less attention has been given to the development of technology to reduce FCCU NO_x emissions. As environmental constraints continue to tighten, this situation is expected to change.

Regenerator NO_x emissions result predominantly from the combustion of nitrogen compounds in the coke coming from nitrogen compounds in the feed, but the oxidation of nitrogen from the regenerator air stream also contributes NO_x. In the latter case, a small amount of O₂ in the regenerator dissociates to highly reactive oxygen atoms, which then attack the otherwise stable N₂ molecule. Increasing the O₂ in the regenerator flue gas from 0.1 to 1.6% has been reported to double NO_x emissions when no CO combustion promoter is present. Adding a platinum-based combustion promoter, which increases the available atomic O₂, can increase the NO_x content much more (46).

Increasing the nitrogen content in the reactor feed generally increases NO_x emissions in the regenerator. Increasing feed nitrogen content from 200–300 ppm to >100 ppm has been reported to increase NO_x emissions from 50 ppm to >450 ppm (46).

Consequently, feed hydrotreatment can be beneficial in reducing regenerator NO_x emissions as well as reducing SO_x emissions. High pressure, 7 MPa (>1000 psig), hydrotreating with a modern nickel–molybdenum catalyst has been reported to reduce total feed nitrogen by 85%, and mild hydrocracking has been reported to reduce feed basic nitrogen by 98% (40). Such treatment is expected to reduce regenerator NO_x emissions up to 85%.

Wet gas scrubbing, which is highly effective for SO_x removal, is much less effective for NO_x removal. Because NO_x in the flue gas is 90–95% NO and because NO has a relatively low solubility in absorbing solutions, little NO_x is removed (47).

The additive approach to reducing SO_x emissions can be either detrimental or beneficial toward NO_x reduction. Early alumina-based SO_x removal additives actually produced substantial increases in NO_x content in the flue gas (48). The more recent spinel-based SO_x removal additives have been reported to reduce NO_x emission by 30% in one commercial trial (49).

Regenerator Operating Parameters

To maximize the performance of an FCCU, most units run at one or more unit constraints. Frequently, one of these constraints is the regenerator temperature, which is set by metallurgical limits for safe operations. Process variables on both the reactor and the regenerator side are thus manipulated to keep the regenerator temperature as close as possible to this regenerator temperature limit.

Changes in feed quality, which will affect the coking tendency of the feed and the coke-making characteristics of the circulating catalyst, influence the regenerator temperature. The refiner can rapidly respond to these changes by manipulating certain independent process variables, which include reactor riser temperature, temperature of the hydrocarbon feed entering the riser, fresh catalyst addition rate, and cooling duty if a catalyst cooler exists. If the change in feed quality is of prolonged duration, the refiner can also change catalyst type.

The heavy material in the reactor feed, which remains as a residue after evaporation and pyrolysis of the oil, is designated as Conradson carbon (ASTM test method D189-76). This residue is frequently used as an indicator of the coking tendency of the feed. Incorporating heavy feedstocks such as vacuum resids into the FCCU feed greatly increases the feed's Conradson carbon content. The influence of increasing resid content on regenerator temperature has been determined and correlated against the feed Conradson carbon content (50). A 2% increase in Conradson carbon can cause a regenerator temperature increase of about 28°C. Other studies indicate that an increase in the resid content of the feed that results in an increase in Conradson carbon from 1.5 to 2.9% produces a regenerator temperature increase of 37°C at constant riser temperature (11).

The presence of contaminant metals on the equilibrium catalyst can significantly increase the catalyst coking tendency, which in turn results in an increase in regenerator temperature if all other factors remain unchanged. As one example, if the metals on an FCCU equilibrium catalyst increased from an equivalent-nickel value of 2000 wt ppm to 3500 wt ppm, the catalyst coke factor would increase 30–50%. If all controllable parameters remained constant, the regenerator temperature would be expected to increase 35–50°C and conversion would drop.

To bring the regenerator temperature down, heat must be taken out of the system. This effect can be achieved by decreased conversion, which decreases the amount of catalytic coke produced, or through physical removal of heat. The heat can be removed by using a catalyst-cooling heat exchanger or by cooling the feed entering the reactor. Typically, decreasing the feed temperature by 28°C decreases the regenerator temperature by 6°C (7).

Decreasing conversion can be achieved by decreasing reactor temperature or by decreasing equilibrium catalyst activity; the latter is more effective in reducing regenerator temperature for a given decrease in conversion. Typically decreasing reactor riser outlet temperature by 8°C decreases conversion 2 to 2S% and decreases regenerator temperature by 6–8°C (7,51). Reducing equilibrium catalyst activity by four numbers, either by decreasing the fresh catalyst addition rate or by using a lower activity fresh catalyst, also reduces conversion by about 2% and decreases regenerator temperature by more than 42°C, depending on the initial temperature (52).

FCCU Regenerator Configuration and Mechanical Hardware

Since the first fluid-bed catalytic cracking unit was commissioned in 1942, more than 300 additional units have been built. During this time, the process has evolved and has seen considerable improvement in mechanical construction, reliability, and process flow. A modern FCCU typically operates continuously for three to four years between turnarounds, during which time 10¹⁰ kg of feedstock are processed and 7 × 10¹⁰ kg of catalyst circulated. Early FCCU designs, (53) were complex compared with the compact configuration of more recent design (Fig. 1).

In the modern unit design, the main vessel elevations and catalyst transfer lines are typically set to achieve optimum pressure differentials because the process favors high regenerator pressure, to enhance power recovery from the flue gas and coke-burning kinetics, and low reactor pressure to enhance product yields and selectivities.

Comparing a modern design with a typically less desirable configuration of the past (54), the principal improvement factors have been aimed toward: reduced catalyst inventory and temperature limitations, enhanced coke-burning kinetics, catalyst and air contacting, and catalyst residence time distribution. New designs have eliminated horizontal transport, long standpipes, additional standpipe aeration requirements, and catalyst fines recycle. During the 1980s, two-stage regenerators and catalyst coolers were commercialized specifically to allow greater unit heat-balance flexibility. These units can effectively process feeds containing a large amount of high boiling, contaminated residual feedstocks.

In the Total R2R two-stage regenerator design (55), the metallurgical temperature limits can exceed the conventional limits of 760°C with the use of refractory-lined external cyclones attached to the second-stage regenerator vessel. Final regeneration temperatures are unconstrained: up to 925°C is attainable. The first regenerator stage operates in a partial-combustion (CO₂ CO), bubbling-bed mode at a maximum temperature approaching 705°C.

Some 60–80% of the total coke and essentially all the hydrogen is burned. The first-stage flue gas leaves the system via conventional two-stage cyclones to a CO boiler. Catalyst then flows by dilute-phase transport to the second-stage regenerator, where the remaining coke is burned at temperatures up to 925°C. This second-stage is designed without any internals in the dilute phase. The second-stage flue gas along with any excess oxygen leaves the system by refractory-lined, single-stage external cyclones and plenum system.

The regenerator configuration of the Ashland RCC unit, which is a reduced crude conversion unit located at Ashland's Catlettsburg, Kentucky refinery, also consists of two distinct bubbling-bed regeneration zones. However, in the RCC regenerator and in the modification of this two-bed concept used in existing unit revamps, both bed temperatures are maintained at <730°C by the combination of heat removal (catalyst coolers) and control of the overall heat of combustion (54,56). The primary zone operates in partial combustion to produce a lower overall heat of combustion via a reduced ratio of CO₂ CO. In this design, additional control is achieved through heat removal in the catalyst cooler, which provides continuous intimate catalyst contact to maintain uniform temperatures of <730°C. The secondary zone operates in total combustion and reduces residual carbon-on-catalyst to less than 0.05 wt %. The excess O₂ and CO₂ leave the system via the upper primary zone. Compared to the R2R design, which has two flue gas lines, this design requires only one flue gas line and one two-stage cyclone separation system. The flue gas containing CO is sent to a waste heat boiler.

INFLUENCE OF REGENERATOR DESIGN ON CATALYST FLUIDIZATION

As regenerator design has improved over the years, various fluidization regimes have been used in the regenerator. These designs include the bubbling bed at low gas velocity, the turbulent bed at higher gas velocity, and the fast-fluidized bed at still higher gas velocity (see FLUIDIZATION).

Bubbling-Bed Design. The bubbling-bed regime ranges from the minimum bubbling velocity (M_{MB}), which typically for FCC-type particles is from 0.006 to 0.03 m/s, up to about 0.3 m/s superficial velocity. Three distinct, yet interchanging, gas phases exist in the bubbling-bed regime: the bubble phase, the emulsion phase, and the gas phase inside the catalyst pores. These phases are all flowing at various relative velocities. Discrete gas bubbles flowing through the bed produce abrupt pressure fluctuations at the bed's surface. The relative fluctuations are set by the bubble frequency or superficial gas velocity.

Units of the past with a typical bubbling-bed regenerator design offered limited solids carryover and transport through the freeboard region. Most of the larger particles that are entrained are returned to the bed through the two-stage cyclone dip legs; the smaller fines, which are less than 10 μm, are mainly carried out with the flue gas.

Turbulent-Bed Design. At the higher gas velocities of the turbulent-bed regime (0.3–1.0 m/s), the distinct bubble phase disappears, and the bulk of the gas flows in a manner described as: "In voids which continually coalesce and split tracing tortuous passages as they rise through the bed" (57). The surface of the upper bed is considerably more diffuse and has reduced pressure fluctuations and substantially higher entrainment of solids into the freeboard region. Because of the higher coke-burning capacity requirements and improved contacting efficiency, the vast majority of commercial regenerators are operating in the turbulent-bed regime. In this configuration, the ultimate regeneration capacity is set by the sharp increase in solid entrainment that occurs as the linear velocity approaches 1.0 m/s and the corresponding effect this air velocity has on the cyclone separation efficiency and dipleg hydraulics (58).

Fast-Fluidized-Bed Design. The fast-fluidized regime (1.0–3.0 m/s superficial velocity) extends into the transport phase, where a sharp increase in the rate of solids carryover occurs as the transport velocity is approached. In the absence of any solid recycle, the bed would rapidly disappear. Beyond this velocity, catalyst fed to the base of the regenerator travels upward in a fully entrained transport flow. The voidage or density of the resulting suspension is dependent not only on the velocity of the gas but also on the solid flow rate. If the solid rate is low, a dilute-phase flow will result. If solids are fed to the regenerator at a sufficiently high rate, eg, by recirculating the solid carried over back to the regenerator, then maintaining a relatively large solid concentration is possible. This condition is referred to as the fast-fluidized bed. At superficial gas velocities substantially higher than the terminal velocity, establishing a high solids concentration, even at high solids loading (transport regime), becomes increasingly more difficult.

The commercial high efficiency regenerator typically operates in the fast-fluidized regime by controlling recirculation of hot catalyst. The catalyst is returned from the exit of the riser back to the combustor inlet via slide-valve-controlled, dense-phase standpipe flow. By the controlled recycle of hot regenerated catalyst, this design configuration allows independent control of combustor inventory (density, residence time), and coke-burning kinetics (temperature and gas solids contacting), as shown in equation 11.

$$\frac{dc_C}{dt} = k_o e^{-\frac{\Delta E}{RT}} c_C P_{O_2}$$

(11)

In comparison, units that are designed with turbulent beds have a lower superficial velocity limit because of solids entrainment and are unable to independently control the entrained solids recycle. The solids loading in the turbulent-bed regenerator configuration are equal to the reactor–regenerator circulation plus the entrained solids via the cyclone diplegs.

Solids Mixing Characteristics. Scale-up factors in fluidized systems are notoriously poor. Therefore, in a commercial design, considerable commercial experience is always used along with a good understanding of fluidization and heat-transfer fundamentals. Scale-up is particularly difficult in the area of solid–gas mixing characteristics, because some commercial regenerators exceed 15 m in diameter. The solid–gas mixing characteristics greatly influence thermal gradients, both interparticle and within the bed; residence-time distribution; and afterburn in the free board and cyclone area.

The mixing characteristics of bubble- or gas-induced solids in the various fluidized-bed regimes have therefore received considerable attention over the years. Mathematical expressions describing the bubble-induced mixing characteristics of solids in fluidized beds show that the axial mixing in a bubbling-bed regenerator is high (150 kg/m²·s) (59).

Although this bubble-induced axial turnover rate of solids is extremely high, the radial mixing characteristics are relatively poor (because bubbles flow vertically) and can lead to distribution problems in the larger diameter bubbling- or turbulent-bed regenerators. An investigation of catalyst mixing patterns in various commercial catalytic cracking units (reactor, regenerator, and stripper sections) was done by using radioisotopes (60). The measured distributions indicate that dense beds in regenerators do approach perfect mixing, but that there are still substantial deviations from perfect mixing attributable to catalyst bypassing and regions of relatively immobile catalyst.

Over the years, to improve the radial mixing characteristics and residence-time distributions (reduce short circuiting) of the turbulent- and bubbling-bed systems, considerable attention has been placed on dual diameter vessels; fluidized-bed length and diameter ratios; air distribution, grid pressure drop, and plugging pattern; cyclone dipleg discharge orientation; and spent catalyst addition and withdrawal points into the regenerator. These addition and withdrawal devices include tangential inlets, swirl distributors, deflector plates, and baffles as well as the entry elevation into the fluidized bed. Consideration of these factors has somewhat improved the situation, but a significant degree of maldistribution still exists within the bubbling-bed regenerators.

In the 1970s, UOP developed the high efficiency combustor to overcome these intrinsic problems. Figure 8 compares theoretical particle residence-time distributions of a turbulent-bed regenerator with those of a modern high efficiency combustor. The basic difference in response curves is a result of both the fluidization regime (fast fluidized) and the solids entry and exit configuration. In the combustor design, a spent catalyst particle cannot possibly leave the regenerator without passing through the dilute-phase combustion zone.

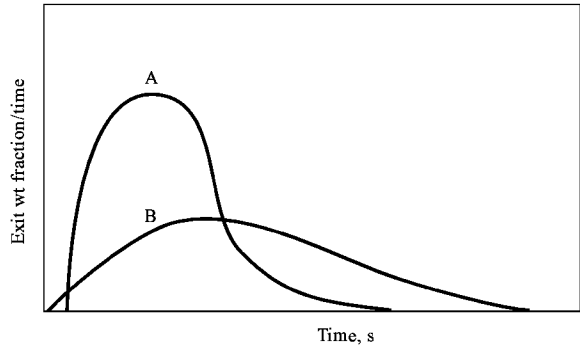


Fig. 8. Theoretical residence time distributions: A, combustor style approach to plug flow; B, turbulent bed (100% backmixed).

The overall benefits of this high efficiency combustor over a conventional bubbling- or turbulent-bed regenerator are enhanced and controlled carbon-burn kinetics (carbon on regenerated catalyst at less than 0.05 wt %); ease of start-up and routine operability; uniform radial carbon and temperature profiles; limited afterburn in the upper regenerator section and uniform cyclone temperatures; and reduced catalyst inventory and air-blower horsepower. By 1990, this design was well established. More than 30 units are in commercial operation.

MECHANICAL HARDWARE

From a mechanical point of view, the FCCU regenerator can be divided into two main sections: the regenerator vessel and its internals, which include the air distributor and the cyclones, the plenum chamber, and catalyst coolers; and the flue gas handling section, which includes power, heat, and particulate recovery systems. Continuous advances in the mechanical design of both these areas have led to significant improvements in overall FCCU reliability, even though processing conditions, at the same time, have become more difficult (harder and denser catalysts, higher regenerator temperatures).

Regenerator Vessel and Internals. The FCCU regenerator is one of the largest vessels in the refinery (up to 18 m in diameter) and operates at temperatures up to 775°C. The regenerator is usually a carbon steel vessel lined with refractory insulation to maintain the wall temperature in the area of 350°C, which is suitable for carbon steel. The usual refractory thickness in the regenerator is 10 cm.

Air Distributor Grid. The function of the FCCU regenerator air distributor is to uniformly introduce O₂ into the regenerator vessel to achieve even burning of coke throughout the regenerator cross section. Every air distributor must be designed for three conditions: start-up, normal operation, and emergency. The actual design temperatures and pressures may vary from unit to unit, depending on the process requirements and configuration. However, these three design conditions are common to all units and must be incorporated into the design. The extreme temperature of the emergency case usually dictates the selection of the distributor metallurgy.

Basically, two types of air distribution systems are used in FCCU regenerators: those that distribute air into the catalyst bed through a perforated plate and those that distribute air through a series of small pipes, known as a pipe grid (61). The pipe grid design is the most commonly used. A typical pipe grid design is shown in Figure 9. The pipe, which is typically constructed of 304 H stainless steel or 1 1/4 Cr–1/2 Mo steel, distributes the air through three or four large laterals into a number of small branches. The grid is designed for a total pressure drop in the range of 3.5 to 7.0 kPa (0.5–1 psi). This pressure drop is set by regulating the air leaving the branch arms through a series of nozzles that point downward. Erosion patterns at the nozzle tip are minimized with the dual-diameter jets that allow the air to develop a full-flow velocity profile across the entire nozzle cross-sectional area prior to exiting. Frequently, some of these nozzles are plugged to prevent jet impingement on adjacent pipes; increase pressure drop; and enhance carbon and air distribution within the bubbling bed. The upper operations limit of the grid is based on jet velocity limitations so as not to cause catalyst attrition. Conversely, the downturn capacity is set by low pressure drop, which can lead to aspiration of catalyst through the peripheral branches. Such aspiration results in severe and accelerated erosion.

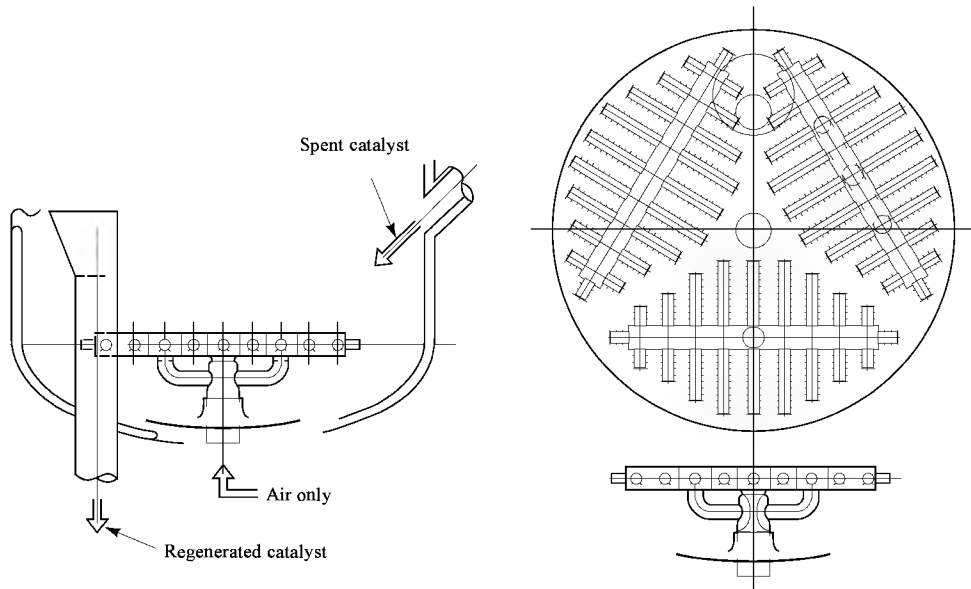


Fig. 9. Regenerator pipe grid air distributor (61).

Cyclones. The high gas velocities inside the regenerator result in considerable catalyst entrainment into the vapor space above the catalyst bed. Cyclones are used to separate these catalyst particles from the exiting regenerator flue gas and return essentially all of these particles to the regenerator bed. In a typical regenerator, the cyclones are installed in sets of two (Fig. 10). In this two-stage arrangement, the gas outlet of the first cyclone is channeled directly to the inlet of the second cyclone. This use of paired cyclones improves the overall separation efficiency and keeps the overall catalyst losses to $<0.3 \text{ kg m}^{-3} \text{ feed}$.

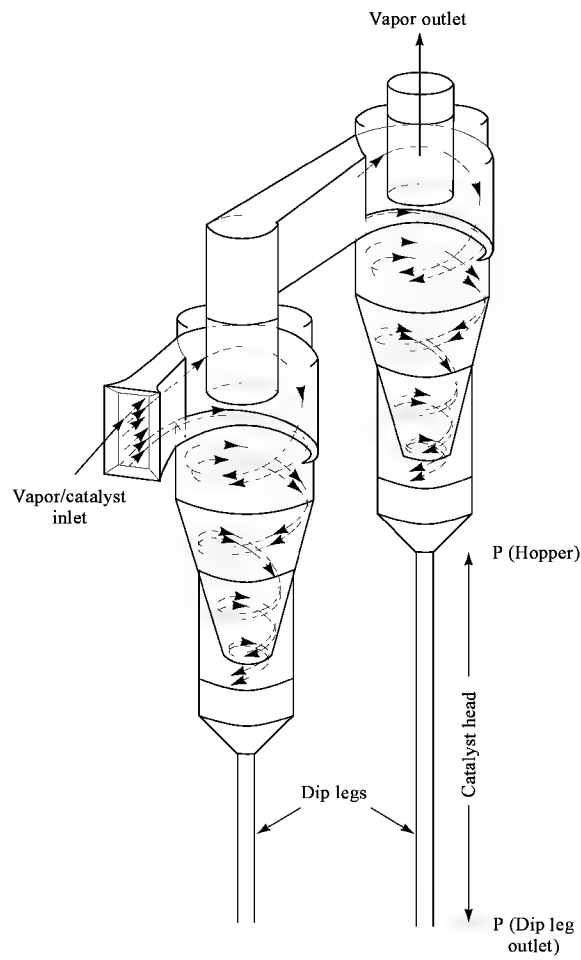


Fig. 10. Cyclone system.

The cyclones are typically designed with diameters of 100–160 cm for ease of maintenance. Cyclone inlet velocities are usually restricted to 18–21 m/s in the first stage and to 20–26 m/s in the second stage to achieve satisfactory pressure drop and erosion characteristics (62). The number of sets of two-stage cyclones thus depends on the total gas flow. Finding room to house all the necessary cyclones within the regenerator frequently requires considerable ingenuity (62).

Catalyst leaving the cyclone flows down the cyclone discharge pipe, known as the dip leg, and builds a layer of catalyst at the bottom of this pipe. Sufficient catalyst head is developed in the dip leg to overcome the cyclone inlet and outlet pressure drop and thus allow the entrained solids to return to the regenerator bed. The second stage sets the required overall dip leg length, and the catalyst seal is maintained with either the dip leg being submerged in the bubbling bed or with a trickle-flapper valve arrangement at the catalyst discharge end. The open bottom, submerged dip leg with only a splash baffle, is used primarily on regenerator first-stage cyclones.

The metallurgy of the cyclone equipment has in recent years focused primarily on type 304 H stainless steel. The 304 H material is durable and easy to fabricate and repair, withstands the high regenerator temperatures, and is oxidation- and corrosion-resistant. Essentially all internal surfaces of the cyclone that are subject to erosion are protected with a 2 cm layer of erosion-resistant lining. When installed and cured, most refractory linings are highly resistant to erosion.

Flue Gas Handling.

Waste Heat Boilers. In a conventional FCCU flue gas system, the regenerator combustion gases pass through two stages of cyclonic separators, a slide valve, orifice chamber, waste heat boiler, and electrostatic precipitator. The slide valve and orifice chamber act in combination to reduce the flue gas to essentially atmospheric pressure.

If the CO is not completely combusted to CO₂ in the regenerator, a CO boiler is used to complete the combustion. The resulting heat of combustion and the sensible heat of the flue gas along with any heat from auxiliary fired fuel are recovered in the form of high pressure steam. When the regenerator is operated in total CO burn, the CO boiler is replaced with either a shell and tube exchanger or a box-type waste heat boiler (see HEAT EXCHANGE TECHNOLOGY).

The shell and tube exchanger, which is a single-purpose piece of equipment, has the standard parts of a normal heat exchanger, but certain parts have been modified to withstand the erosive service of the particulate-laden flue gas stream. This design has the limitation of being able to produce only saturated steam. The flue gas leaves the regenerator at temperatures up to 760°C and exits the exchanger at approximately 315°C. The flue gas then proceeds through the pressure-control slide valve and orifice chamber, which reduces its pressure to atmospheric prior to entering the electrostatic precipitator or stack.

The connection box cooler receives regenerator flue gas after it has been reduced to essentially atmospheric pressure. This arrangement is not limited to the production of saturated steam. Any number of coils can be installed in the box, and normally both steam-generating and superheater coils are present. The tube temperatures within the box must be maintained above the SO₃ dew point of 150–175°C to prevent sulfuric acid corrosion (63).

The principal differences between the shell and tube and the connection box designs may be summarized as follows:

	Shell and tube	Box
flue gas pressure	138–276 kPa	atmospheric
type of steam	saturated	saturated plus superheated

steam pressure limit

3500 kPa

none

Power and Particulate Recovery. Another technique uses the energy in the hot flue gas leaving the regenerator to pass the gas through an expansion turbine and thereby generate usable power or electricity (64). The power train typically consists of the power recovery or expander turbine, a motor or generator, the air blower, and a steam turbine. All of this equipment is mounted in tandem. Flue gas from the regenerator enters the third-stage separator, where 95% of the 10 µm plus material is removable. In the separator, catalyst is removed from the flue gas by passing the catalyst-entrained gas stream through a large number of tube assemblies, which contain specially designed swirl vanes. The swirl vanes impart a strong centrifugal force that separates out the catalyst particles (64). Table 3 shows typical particle separation data for this high efficiency, third-stage separator (65). Overall efficiency depends on the particle-size distribution of the catalyst leaving the regenerator cyclones. A separator efficiency of 70% is typical for handling catalyst fines from a highly efficient regenerator cyclone. Less efficient cyclones feeding coarser material to the separator results in a 90% separator efficiency.

Table 3. Particle-Size Distribution from a Shell Third-Stage Separator^a

Particle size	Approximate range, %	
	Entering separator	Leaving separator in flue gas
greater than 40 µm	3–16	
20–40 µm	23–54	
10–20 µm	34–22	3
4–10 µm	14–8	5–17
2–4 µm	14–3	15–40
0–2 µm	17–3	80–40

^a Ref. 65.

Recovered catalyst and blowdown gas (~3% of the flue gas) exit from the bottom of the separator to an electrostatic precipitator or to a small, fourth-stage cyclone for further concentration of catalyst fines. The flue gas, with 70–90% of the catalyst particles removed, passes from the separator into the power expander.

The expansion turbine converts the dynamic energy of the flue gas into mechanical energy. The recoverable energy is determined by the pressure drop through the expander, the expander inlet temperature, and the mass flow of gas (66). This power is then typically used to drive the regenerator air blower.

The expander turbine is designed to minimize the erosive effect of the catalyst particles still remaining in the flue gas. The design ensures a uniform distribution of the catalyst particles around the 360° annulus of the flow path, optimizes the gas flow through both the stationary and rotary blades, and uses modern plasma and flame-spray coatings of the rotor and starter blades for further erosion protection (67).

FCC Catalyst Coolers. Heat-removal systems have been used in commercial FCCUs since the early 1940s. The three basic designs are internal regenerator bed coils, external coils with dilute-phase upflow, and external coils with dense-phase downflow.

Internal Regenerator Bed Coils. Internal coils generate high overall heat-transfer coefficients [550 W (m²·K)] and typically produce saturated steam up to 4.6 MPa (667 psi). Lower heat fluxes are attained when producing superheated steam. The tube banks are normally arranged horizontally in rows of three or four, but because of their location in a continuously active bubbling or turbulent bed, they offer limited duty flexibility with no shutdown or start-up potential.

External Dilute-Phase Upflow Cooler. The external dilute-phase upflow design (68) offers some control in the range of heat removal duties but generates relatively low heat-transfer coefficients [60–170 W (m²·K)]. This design substantially increases the surface area requirement and thereby reduces the ultimate duty that can be achieved from a single bundle. In addition, poor mechanical reliability has been continuously experienced because of excessive erosion at the lower tube sheets as a result of the high catalyst fluxes and gas velocities imposed.

External Dense-Phase Downflow and Backmixed Cooler. This relatively recent design improvement has achieved excellent mechanical reliability and the same or better on-stream efficiency (three years) as many of the other mechanical components of the FCC system. The design also has a wide range of easily controlled heat removal duties. This unique all-vertical bundle design allows either a backmixed or flow-through configuration (Fig. 11). The bayonet tube design uses forced water circulation and allows for catalyst to flow on the shellside of the bundle. Both the catalyst flux and aeration velocities are controlled at low levels and at the same time controllably produce a wide range of heat-transfer coefficients. Concerns regarding erosion or differential are minimal. The independently controlled catalyst flow produces a countercurrent gas (bubble-phase) and solid flow. Typically, a single cooler can be operated and controlled anywhere within a 6–50 × 10⁶ watt saturated-steam production range.

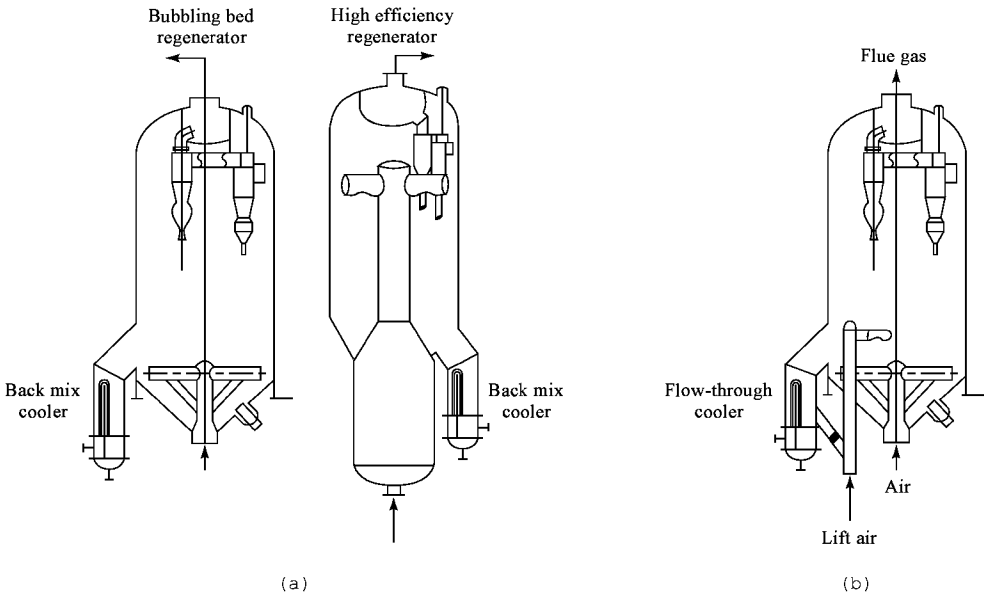


Fig. 11. Catalyst cooler configurations where (a) is backmix cooler and (b) is flow-through catalyst cooler (69).

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NOBLE AND BASE METAL CATALYSTS

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Noble Metal Catalysts

Heterogeneous catalysts containing noble metals, such as platinum, are widely used in the petroleum refining industry for a large variety of hydrocarbon conversion processes. The products made by these processes, such as motor fuels and petrochemicals, are of immense economic value. Processes of commercial importance that use platinum catalysts include reforming of low octane naphtha to produce high octane gasoline, reforming to produce aromatics, paraffin isomerization, xylene isomerization, hydrogenation, and dehydrogenation.

Catalysts in this service can deactivate by several different mechanisms, but deactivation is ordinarily and primarily the result of deposition of carbonaceous materials onto the catalyst surface during hydrocarbon charge-stock processing at elevated temperature. This deposit of highly dehydrogenated polymers or polynuclear-condensed ring aromatics is called coke. The deposition of coke on the catalyst results in substantial deterioration in catalyst performance. The catalyst activity, or its ability to convert reactants, is adversely affected by this coke deposition, and the catalyst is referred to as spent. The coke deposits on spent reforming catalyst may exceed 20 wt %.

The original performance of the fresh catalyst can be successfully restored by proper regeneration to remove this coke. Regeneration allows continued use of the same catalyst for many years. Thus even expensive and sophisticated catalysts can become economical for commercial use in petroleum refining.

DEACTIVATION

The performance of catalysts in general is measured in terms of activity, selectivity, and stability. Activity is a measure of the ability of the catalyst to convert hydrocarbon reactants into the desired products at a specified temperature, pressure, contact time, and so forth. Selectivity refers to the amount of the desired product obtained as a function of the amount of reactants charged or converted. Stability is a measure of the rate of change of activity or selectivity with time. The deactivation of a catalyst refers to a decline in the activity or selectivity of the catalyst (1–5). In naphtha reforming, a hydrocarbon feed stream containing paraffins and naphthenes is subjected to conditions that promote dehydrogenation of naphthenes to aromatics, dehydrocyclization of paraffins to aromatics, isomerization of paraffins and naphthenes, and hydrocracking of naphthenes and paraffins to produce a high octane or aromatics-rich product stream. Significant volumes of hydrogen are produced as an additional valuable by-product.

Catalysts used in the petroleum refining industry for naphtha reforming are platinum or platinum with additional transition-element promoters and a halogen, such as chloride. These components are supported on formed particles of high surface area gamma alumina. The catalysts are bifunctional: acidity is provided by the halogen component, and functions such as hydrogenation and dehydrogenation are provided by the platinum component or by platinum modified with an additional component such as rhenium or other Group (IVA) elements. For example, a typical catalyst composition may be 0.25 wt % Pt, 0.25 wt % Re, and 1.0 wt % Cl supported on high purity extruded gamma alumina with a surface area of 180 m²/g to 200 m²/g.

Naphtha reforming catalysts can become deactivated by several different phenomena, including: (1) *coke deposition*, which covers the catalytic surface and thus prevents access by reactants. This phenomenon is the most common and unavoidable cause of the deactivation of reforming catalysts. The rate of coke deposition is a function of the feedstock quality, the operating conditions of the process, and the catalyst formulation; (2) *plant upsets*, such as the introduction of feedstock containing hydrocarbon components with a high boiling point or high sulfur, loss of recycle hydrogen, or severe water or chloride upsets; (3) *agglomeration of the platinum on the catalyst surface*. This reaction provides a decreased catalytic metal surface area and decreases the beneficial effect of bimetallic platinum modifiers. Platinum agglomeration on modern catalysts usually occurs during regeneration and not during hydrocarbon processing; (4) *fouling by corrosion products*, such as scale from commercial vessels and heat exchangers. This problem is ubiquitous in commercial service, but the elements deposited are not ordinarily in a catalytic form and have little effect on the catalyst performance; and (5) *poisoning* by a wide variety of undesirable feed components, such as sulfur, alkali metals, lead, or arsenic. This poisoning can deactivate either the metal or acid functions or both on the catalyst. As a result, catalyst selectivity is affected, and the catalyst usually deactivates even more quickly. Today, these feedstock impurities are typically reduced to low levels by hydrotreating the naphtha and thus are rarely the cause of deactivation.

REGENERATION

Regeneration of noble metal catalysts to remove coke deposits can successfully restore the activity, selectivity, and stability performance of the original fresh catalyst (6–17). The basic steps of regeneration are carbon burn, oxidation, and reduction. Controlling each step of the regeneration procedure is important if permanent catalyst damage is to be avoided.

REGENERATION PROCESSES

Three different *in situ*, or on-site, techniques are widely used to regenerate naphtha-reforming catalysts: CCR (continuous catalyst regeneration), fixed-bed semiregenerative regeneration, and cyclic, or swing, reactor regeneration. These techniques include the general steps of coke combustion under conditions of controlled oxygen and controlled temperature, platinum redispersion and chloride adjustment, and hydrogen reduction.

Ex situ, or off-site, regeneration of noble metal catalysts is not commonly practiced by commercial petroleum refiners because it requires either an extended period with the process shut down or requires that a spare load of costly catalyst, which would only be used for a fraction of the time, be purchased and kept available.

Continuous Catalyst Regeneration. The state-of-the-art method of reforming catalyst regeneration is continuous circulation of the catalyst through the process reactors and a regeneration vessel as a moving bed, as is done in the UOP CCR Platforming process shown in Figure 1 (18–20). The catalyst, typically in the form of 1.6 mm diameter spheres, is transferred by the gravity flow of the particles through the reactors and regenerator vessels. A gas stream is used to entrain and lift the catalyst for transfer from the bottom of one section to the top of the next. Appropriate computerized valves and lock hoppers control the catalyst environment and the catalyst circulation rate. The catalyst within the regenerator is contained in an annular space, which allows for effective contacting of the catalyst with the various required regeneration gases. The regenerated catalyst is continuously returned to the process reactors. Two licensors of technology with continuous regeneration are UOP and Institut Francais du Pétrole (IFP).

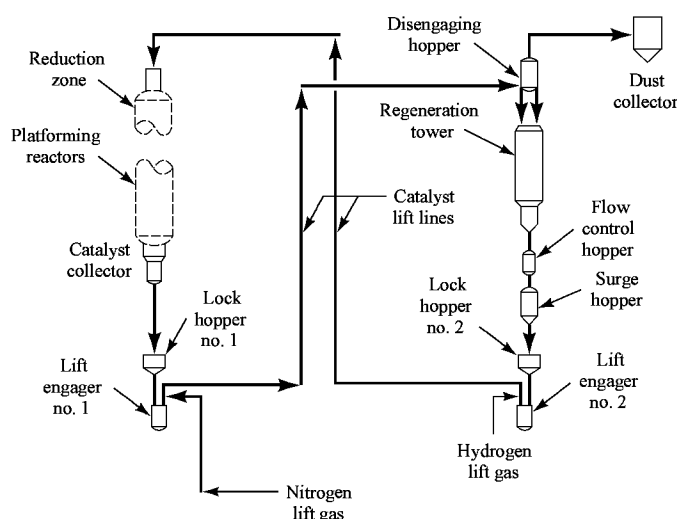


Fig. 1. UOP CCR Platforming catalyst regeneration section.

The UOP CCR method of regeneration provides continuous process performance that is near that of fresh, undeactivated catalyst by allowing regeneration with such frequency that catalyst deactivation is minimized. The CCR technique allows the operation of the reforming process at higher severities, that is, high temperature and high product octane number, than would ordinarily be possible because of rapid catalyst deactivation. Reforming at low pressure, 0.45 to 0.96 MPa (65–139 psi) is made possible by CCR technology. The CCR technology improves the yield of the gasoline product in naphtha reforming by several percent relative to conventional fixed-bed, semiregenerative reforming at 1.8 to 2.2 MPa (261–319 psi). A higher octane reformate is produced as well as a large quantity of relatively high purity hydrogen, which can be used as a feedstock for hydrogen-consuming processes in the refinery, such as hydrocracking and hydrotreating units.

The catalysts used in this CCR commercial service must meet several stringent physical property requirements. A spherical particle is required so that the catalyst flows in a moving bed down through the process reactors and regenerator vessel. These spheres must be able to withstand the physical abuse of being educated and transferred by gas flow at high velocity. The catalyst particles must also have the proper physical properties, such as particle size, porosity, and poresize distribution, to achieve adequate coke combustion kinetics.

The first step in regeneration, combustion of the coke that has accumulated on the catalyst surface, is done in a carefully controlled manner by contacting the catalyst at elevated temperature with a gas containing a low concentration of oxygen. Controlling the oxygen level is of critical importance to avoid damage to the catalyst. The use of a gas with a low oxygen content allows control of the magnitude of the combustion exotherm and therefore control of the maximum temperature to which the catalyst is exposed. Simulations show that the use of an oxygen level that is too high, for example, greater than about 2.0 mol %, will result in an uncontrolled runaway exotherm; the heat is generated faster than it can be carried away by the flowing combustion gas. Temperatures in excess of 1000°C may result, and these temperatures damage not only the catalyst but also the regeneration equipment itself.

Support-phase changes or loss of surface area are, of course, irreversible, and replacement of the catalyst may be appropriate. Catalyst damage may take the form of phase changes to the alumina support from gamma to theta or alpha phase. The last is catalytically inert because of insignificant surface area. Theta alumina has a low surface area (<100 m²/g) relative to gamma alumina (180 m²/g) and has poor halogen retention.

Some loss of alumina surface area is observed even in the case of well controlled regenerator operations because of the unavoidable hydrothermal treatment of the catalyst during coke combustion. This loss of surface area is usually insignificant for a single regeneration, but over the course of as many as 200 to 250 regenerations in a commercial process, the catalyst surface area will slowly decline from about 180 to 120–130 m²/g as measured by BET nitrogen adsorption isotherm. At this point, although the catalyst performance has not necessarily declined, the halogen (chloride) retention capability of the catalyst is poor, and additional chloride in the regenerator is required to achieve the level needed for acceptable performance.

Catalyst damage may also take the form of platinum sintering or agglomeration as a result of hydrothermal treatment at elevated temperatures. The strong metal and support interaction that exists between platinum and gamma alumina is decreased at these conditions. The result is that the platinum on the catalyst mobilizes and agglomerates into large crystallites (>3 nm). Fresh reforming catalyst typically has an excellent surface platinum dispersion. The platinum crystallites are too small (<2 nm) to be detected by conventional x-ray diffraction analysis or even by much more sophisticated techniques, such as scanning transmission electron microscopy (STEM). Gas adsorption analyses suggest that 100% of the platinum is accessible to the reactants. After a poor regeneration, however, the platinum may be agglomerated into crystallites of sufficient size to significantly decrease both the catalytic metal surface area and the beneficial effect of bimetallic platinum modifiers. The platinum has a greater tendency to agglomerate and form large diameter crystallites on a catalyst with a low surface area. Platinum agglomeration is preventable by avoiding the high peak temperatures associated with coke combustion exotherms. Platinum agglomeration is reversible by proper chlorination if the platinum crystallites are not excessively large (>30 nm).

The next step of the UOP method of CCR regeneration is oxidation and chlorination. In this step, the catalyst is oxidized in air at about 510°C. A sufficient amount of chloride is usually added as an organic chloride, such as trichloroethane, to restore the chloride content and acid function of the catalyst to that of the fresh catalyst. If the platinum crystallites are smaller than about 10 nm, sufficient chlorine is present in the gas to completely redisperse agglomerated platinum on the catalyst, as a result of the Deacon equilibrium:



The catalyst is then transferred back to the first process reactor and is reheated to the reforming process temperature at the reactor inlet using a flow of hydrogen-rich process recycle gas, thereby achieving reduction of the platinum to a catalytically active state.

Fixed-Bed Semiregenerative Process. Most catalytic reforming processes use a series of reactors containing a fixed bed of catalyst in a variety of configurations. Worldwide, as many as 800 to 1000 commercial semiregenerative reforming process units are in operation. Catalyst in these process units is regenerated only periodically, typically once or twice per year, in anticipation of the higher gasoline production demands of the summer months; hence the term semiregenerative. The process conditions typically include 2.2 MPa (319 psi) and 510°C. As the catalyst deactivates, the reactor temperatures are periodically increased to maintain the desired product octane. The bimetallic catalysts typically used contain platinum and rhodium promoters at 0.2 to 0.8 wt %. These promoters are supported on spherical or extruded particles of gamma alumina and contain about 1.0 wt % chloride. After a deactivation of about 15 to 22°C, the catalyst may have accumulated as much as 20 wt % coke.

The need for commercial reforming catalyst regeneration is normally determined by one of the following criteria: the reactor temperature limit has been reached, and target product octane cannot be achieved; the product yield has declined to an uneconomical level; the firing limit of the charge heater has been reached; or refinery scheduling requirements must be met. The first three limits are primarily a result of catalyst deactivation because of carbon deposition. The rate of this deposition is dependent on the feedstock quality, process operating conditions, and catalyst formulation.

The semiregenerative procedure for catalyst regeneration varies slightly between catalyst vendors; however, it typically follows these general steps: plant shutdown, carbon burn, oxidation and chlorination, nitrogen purge, reduction, and plant start-up. During the plant shutdown, liquid hydrocarbons

are drained, and the catalyst is stripped of volatile hydrocarbons to shorten the carbon burn step as much as possible. In anticipation of the carbon burn step, the catalyst and reactors are then purged with nitrogen to remove any trace of hydrogen.

The conditions for the carbon burn step are typically less than about 1.0 mol % oxygen, 400°C inlet temperature, 455°C maximum outlet temperature, which is controlled by adjusting the oxygen content of the circulating gas, and 0.45 to 2.2 MPa. The carbon burn is considered to be complete when no exotherm is observed for several hours. The oxygen concentration at all reactor inlets and outlets should be equal at this point.

Oxidation and chlorination of the catalyst are then performed to ensure complete carbon removal, restore the catalyst chloride to its proper level, and maintain full platinum dispersion on the catalyst surface. Typically, the catalyst is oxidized in sufficient oxygen at about 510°C for a period of six hours or more. Sufficient chloride is added, usually as an organic chloride, to restore the chloride content and acid function of the catalyst and to provide redispersion of any platinum agglomeration that may have occurred. The catalyst is then reduced to return the metal components to their active form. This reduction is accomplished by using a flow of electrolytic hydrogen or recycle gas from another Platforming unit at 400 to 480°C for a period of one to two hours.

For some catalyst compositions, presulfiding the catalytic metals is required prior to the introduction of feedstock to decrease the initial cracking activity of the freshly reduced catalyst metal surface. This presulfiding phenomenon is clearly differentiated from the harmful sulfur contamination of the feedstock during processing because it is performed on the clean, freshly reduced catalyst in the absence of feedstock. Unsulfided, reduced platinum or platinum and rhenium catalysts have the potential to crack naphtha completely to methane via alpha-scission. This highly exothermic demethylation or hydrogenolysis reaction can accelerate rapidly as the temperature increases, causing a temperature runaway in the reactor. This condition is readily avoided by the presence of a small quantity of hydrogen sulfide in the system.

Cyclic, or Swing, Reactor Regeneration. A number of licensors, including Amoco (Ultraforming), Shell, and Exxon (Powerforming), have cyclic, or swing, regeneration. In this scheme, typically five process reactors are used in a cyclic manner. While one of the four reactors normally in process use is being regenerated, a fifth, or swing, reactor is substituted. Commercially catalytic reforming is achieved using a series of sequential reactors to allow reheating of the reactants between reactors. The first, or lead, reactor primarily catalyzes the facile, highly endothermic reaction of naphthene dehydrogenation and usually contains only about 10% of the total catalyst in service. This reactor shows the least deactivation and is regenerated only every few weeks. The final, or tail, reactor catalyzes the paraffin dehydrocyclization reactions, which are much more difficult and therefore may require weekly regeneration. This method has a shortened performance cycle duration relative to semiregenerative reforming. Thus the unit can operate at a lower pressure condition of 1.5 to 1.8 MPa, rather than 2.2 MPa.

The regeneration procedure used for the cyclic process is essentially the same as for semiregenerative reforming. The cyclic procedure entails a brief nitrogen purge of the catalyst after the oxidation–chlorination step to remove oxygen followed by the introduction of hydrogen to reduce the catalyst. During the nitrogen purge sufficient time may not be allowed to remove water chemisorbed on the catalyst during the oxidation–chlorination step. Subsequent reduction of the platinum on this insufficiently dried catalyst, using hydrogen gas in a wet atmosphere, may result in undesirable platinum agglomeration. These procedures can result in the reforming process cycle operating with recycle gas having a water level of 80 ppm or more rather than the preferred <20 ppm. High water levels can have a deleterious effect on the catalyst activity, selectivity, and stability. In response to this problem, some refiners use dryers on the recirculated gas during the catalyst regeneration.

Base Metal Catalysts

Heterogeneous catalysts containing non-noble or base metals such as nickel, cobalt, molybdenum, and tungsten are commonly used in the petroleum refining industry for a large variety of hydrocarbon conversion processes. Processes of commercial importance that use such catalysts include hydrotreating, hydrocracking, and residuum cracking, desulfurization, and demetallation. Hydrotreating removes sulfur, nitrogen, oxygen, and metallic impurities from petroleum distillates to make them suitable for further processing. The hydrocracking process selectively converts distillates; vacuum gas oils; and demetallized, deasphalted oils into higher value, lower boiling products such as liquefied petroleum gas (LPG), naphtha, jet fuel, diesel fuel, and lubricating oils. The three principal licensors of hydrocracking technology are UOP, Chevron, and Unocal.

Hydroprocessing catalysts can deactivate by several different mechanisms, including fouling by carbonaceous deposits, sintering of the metals on the catalytic surface, and deposition of reversible and irreversible poisons on the catalyst. If deactivation is primarily the result of carbonaceous deposits, as in the case of the hydrocracking process, the performance of the original fresh catalyst can be substantially restored by a regenerative oxidation treatment to remove this deposit. The treatment is preferably done *ex situ* for a variety of compelling reasons.

In many of the other processes that use base metal catalysts, irreversible poisoning of the catalyst occurs as a result of deposition of metal contaminants from the process feedstock onto the catalyst surface. These catalysts are not considered to be regenerable by ordinary techniques.

The following discussion of base metal catalyst regeneration uses the hydrocracking process and catalyst, specifically UOP HC Unibon, as an example.

PROCESS AND CATALYST DESCRIPTION

Hydrocracking processes in commercial use today are categorized as single-stage, series-flow, and two-stage designs. Each process presents different operating environments for the catalysts, and the net result is varying degrees and types of deactivation. In the environment of the first reactor, the catalyst may be exposed to raw feedstock containing organic sulfur and nitrogen compounds, heavy refractory components, and possibly small amounts of metal poisons. The catalyst in this reactor must convert the organic nitrogen, sulfur, and oxygen compounds to generate ammonia, hydrogen sulfide, and water. In addition, some aromatic components are hydrogenated, and any metal contaminants in the feed are scavenged. Therefore, in the single-stage and series-flow operations the catalyst must operate in the presence of ammonia, hydrogen sulfide, and water. In the two-stage process, these contaminants are scrubbed from the gas phase, and so the second-stage catalyst is exposed to a relatively clean, contaminant-free atmosphere.

Catalysts in use in the hydrocracking process are bifunctional and contain an acidic carrier, such as alumina, silica–alumina, or zeolites such as Y-type, and a base metal or metals hydrogenation component. The relative strength of these two functions and their exact nature depends on their particular use. Optimized catalysts for each of these environments have different compositions. Combinations of cobalt or nickel combined with molybdenum or tungsten are the most commonly used hydrogenation components. The catalysts are typically in the form of 1.6 mm spheres or extrudates. The exact catalyst formulations are considered to be highly proprietary by the catalyst suppliers and usually are not readily available. However, this information is not essential to a description of the catalyst regeneration.

DEACTIVATION

In hydrocracking, the following factors can result in catalyst deactivation (21): coke deposition, adsorption of heavy organic contaminants, sintering and agglomeration of metal sulfides, degradation of support structural integrity, deposition of feedstock metal contaminants, and deposition of metallurgical degradation products.

Pretreating catalysts are subject to all these effects, but the second reactor of a series-flow design is likely to be affected by only the first four. Second-stage hydrocracking catalysts are also subject to only the first four deactivating factors. However, in this case the low concentrations of ammonia and water in the process recycle gas permit lower process operating temperatures and consequently much slower catalyst deactivation as a result of metals sintering or structural degradation of the support. This milder operating environment makes these second-stage catalysts most appropriate for regeneration.

The coke or carbon deposition on the catalyst during feedstock processing may consist of oligomers of small straight-chain hydrocarbons, fused-ring polynuclear aromatics, or large sheets of disordered graphitelike materials. The refractory graphitic coke, which requires more severe regeneration conditions for removal, is deposited at conditions of higher temperature severity, such as a first-stage reactor environment. The coke on spent second-stage hydrocracking catalyst is typically about 15 to 20 wt %.

Catalyst deactivation can be partially counteracted during the process operation by temperature increases and reduction in feed rate, but these changes are limited by metallurgical constraints and economics, respectively. A decision between catalyst replacement or regeneration is made on the basis of the probability of catalyst performance recovering to an acceptable level. This judgment can often be made from the operating history and feed quality history of the unit. Severe temperature excursions or the presence of high levels of metal contaminants in the feedstock can cause permanent, irreversible damage to the catalyst and thus necessitate its replacement. If an *ex situ* regeneration is to be performed, the used catalyst can be analyzed as discussed in the next section.

EX SITU VERSUS *IN SITU* REGENERATION

Ex situ, or off-site, regeneration of base metal catalysts is a service offered by several vendors worldwide, including Catalyst Recovery, Inc., of Lafayette, Louisiana, and Medicine Hat, Alberta, Canada; Catalyst Recovery, Europe of Rodange, Luxembourg; Nippon CRI of Miyako, Japan; Englehard (formerly Filtrol) of Salt Lake City, Utah; Eurecat, U.S., of Pasadena, Texas; and Eurecat, SA of La Voulte, France (22–28).

Ex situ regeneration of base metal catalysts is almost exclusively practiced by the refining industry, for a variety of reasons: (1) decreased process downtime if a spare catalyst bed is available; (2) no risk of damage to process equipment; (3) lower risk of damage to catalyst; (4) ability to evaluate the regenerability of the catalyst; (5) ability to evaluate the success of regeneration; (6) environmental requirements (vendors' concerns); (7) greater operator experience with critical regeneration procedures; and (8) lower reactor pressure drop after regeneration and screening because of fines removal.

One of the few disadvantages of off-site regeneration is the necessity to inventory a spare charge of catalyst to replace the loading sent for regeneration. The expense of the purchase and storage of this extra catalyst may lead a small refiner to choose the higher risk, inadvisable *ex situ* regeneration without a spare loading of catalyst or *in situ* regeneration.

Catalyst Regenerability Assessment. When the catalyst has been removed from the reactor, it then becomes available for a laboratory analysis to assess the probability of success of a regeneration procedure. Carbon and sulfur levels are determined. For zeolitic catalysts, x-ray diffraction analysis can be used to assess the zeolite crystallinity, which determines the extent of hydrothermal damage to the zeolite structure of the catalyst that may have occurred during processing. A surface area analysis of spent, coked catalyst is ill-advised because of the obvious effect of the presence of coke on adsorption isotherm analysis. The top catalyst beds of pretreater reactors should be checked for metal contaminants, such as sodium, vanadium, iron, and arsenic. The presence of high levels of these contaminants suggests that regeneration may not successfully restore catalyst activity.

The *ex situ* regeneration vendor may be provided with a representative sample for a laboratory regeneration trial. This trial can be followed by physical and chemical property analysis to determine the potential for recovering catalyst performance and to judge the success of the commercial regeneration if it is performed. Based on this laboratory regeneration, the vendor may offer a guarantee of regenerated catalyst properties, such as 0.75 maximum wt % carbon, 0.75 maximum wt % sulfur, 90% of the surface area of the laboratory regenerated sample, etc. Other indicators of importance are zeolite properties, metal dispersion, physical strength, color and appearance, size distribution, and fines content of the catalyst. Many of these properties of the catalyst should be considered necessary but not sufficient because acceptable values of the measurable physical and chemical properties of the catalyst do not ensure good catalyst performance. In the final analysis, the laboratory-regenerated catalyst activity and selectivity performance can be predicted best by pilot-plant evaluation using process conditions and feedstocks appropriately selected to correlate with the intended commercial use. However, such pilot-plant evaluation can be prohibitively costly and time consuming, and requires considerable knowledge if it is to be performed correctly.

Ex Situ Regeneration Procedures. The choice of optimum conditions for regeneration is dependent on the type of catalyst and its service history. Spent catalysts with completely different regeneration characteristics may result from differences in feedstock, process unit operating conditions, unit upsets, operating cycle length, and so forth. Because of this variability in the conditions of coke deposition, the coke should be characterized analytically. Chemical analysis can be made of the coke's hydrogen content, which affects its heat of combustion and the minimum ignition temperature required to initiate combustion. Thermogravimetric analysis (tga) and differential thermal analysis (dta) can be used to determine the temperatures at which sulfur and carbon combustion is initiated and the magnitude of exothermicity to be expected. The kinetics of coke combustion can be determined by using tga to generate an Arrhenius plot, which indicates the degree of diffusion-limited reaction to be expected. This analysis may be of most interest for catalysts containing a zeolite component, which has a more microporous nature than amorphous catalysts and consequently demonstrates a greater diffusion limitation.

In general, the following steps are used to ensure optimum regeneration and catalyst performance recovery: a low temperature first pass to remove low boiling point hydrocarbons and other volatile matter, an initial combustion step to remove a portion of the sulfur and carbon, and a final combustion step to remove the remaining carbon to the target level.

The Nippon CRI procedure uses enclosed moving-belt calciners (Fig. 2). The catalyst is conveyed on a stainless steel mesh belt through gas-fired heating zones in which the catalyst is contacted with the appropriate gas. The independently heated zones, variable belt speed, inlet and outlet flow dampers, and choice of gas addition of such equipment allows the control of temperature, time, gas flow rate, and gas composition. The initial treatment is intended to volatilize residual hydrocarbons from the catalyst. These hydrocarbons can be removed without combustion by heating the catalyst in an inert atmosphere, such as nitrogen, or by cautiously heating the catalyst in an oxygen-containing stream while avoiding the initiation of combustion. The subsequent highly exothermic carbon-burning step is controlled by limiting the addition of fresh air to the oven. Temperatures are measured using thermocouples in contact with the moving catalyst bed or suspended closely above it. Complete carbon burning may require more than one pass through the oven if the maximum temperature is to be adequately controlled to avoid damage to the catalyst.

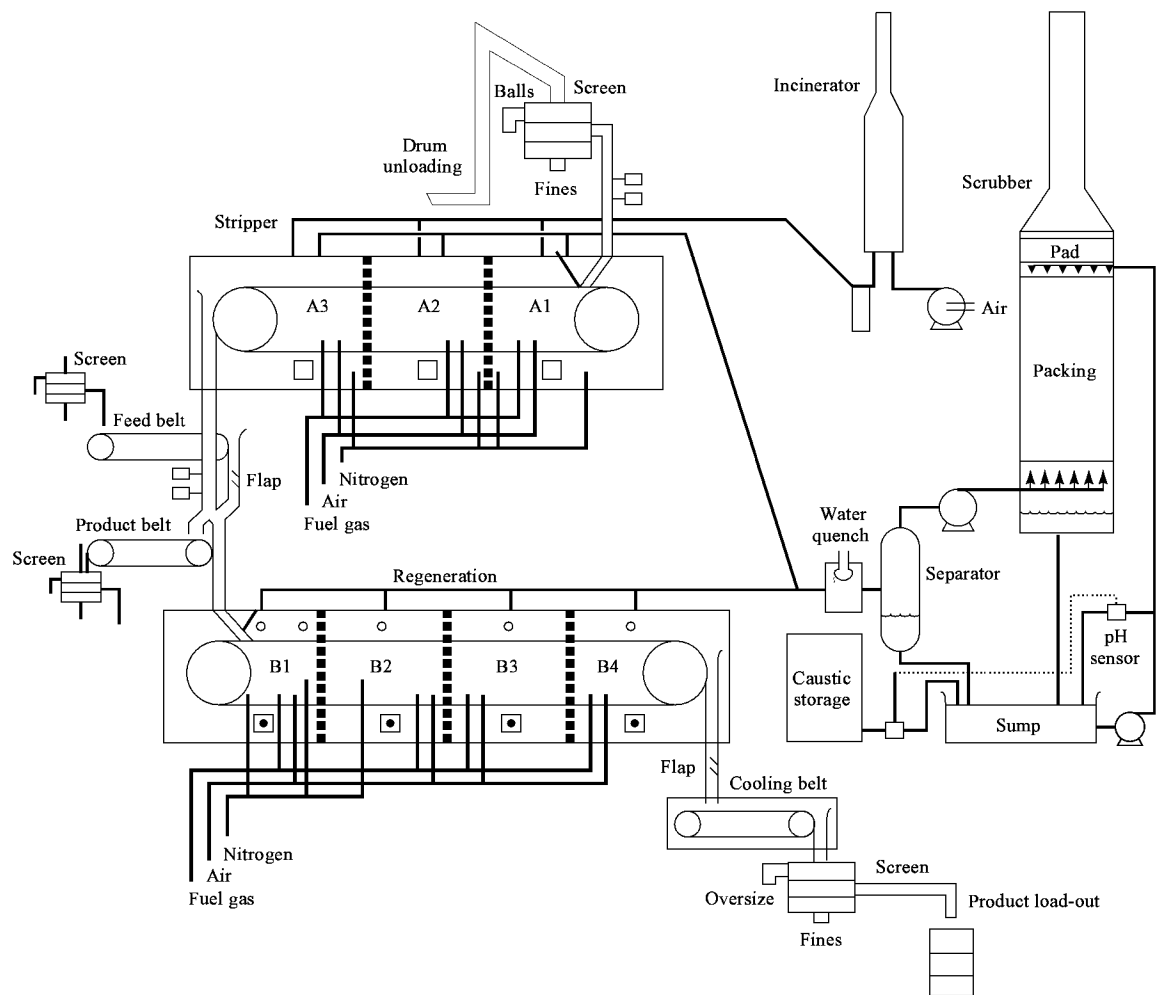


Fig. 2. Moving-bed calciner regeneration of base metal catalysts.

The Engelhard and Eurecat regeneration processes use rotary calciners rather than moving-bed belt calciners. The catalyst is charged into conical-shaped rotating drums and is lifted and tumbled by a series of louvers as it is conveyed to the discharge end. A heated, forced air draft flows between the louvers and through the tumbling catalyst bed along the length of the unit. Temperature is measured using trailing thermocouples in contact with the catalyst bed or by pyrometers mounted at the end of the unit.

The skill and effectiveness of the operators in implementing the regeneration is critical to the final outcome. For example, if combustion is allowed to occur during the initial step when the catalyst may contain adsorbed hydrocarbons that are hydrogen rich and have a high heat of combustion, an uncontrolled runaway reaction can occur. This reaction exposes the catalyst to high temperatures and excessive steam levels. These conditions can result in irreversible sintering of the metal components of the catalyst as well as a loss of surface area or zeolite crystallinity. Both results are likely to have a significant and adverse effect on subsequent catalyst performance.

In the second phase, performed at a maximum temperature of about 370°C, the sulfur and a portion of the coke are removed by combustion. The rate and exothermicity are controlled by limiting the flow of combustion gas through the catalyst. Spent base metal catalysts may have sulfur levels of from 6 to 12 wt % in the form of metal sulfides. A high degree of sulfur removal must be achieved in these first two regeneration steps to avoid the formation of sulfate on the support during the final combustion step. Such a formation causes a loss of catalyst activity.

In the final step of regeneration, higher temperatures are employed to complete carbon combustion. The maximum temperatures allowed depend on the catalyst composition. A temperature of 530°C may be acceptable for catalysts containing metal components of cobalt and molybdenum. However, 530°C may not be acceptable for nickel catalysts, which can irreversibly form surface pseudo-nickel aluminates at elevated temperature. These aluminates are catalytically inferior. Here, as in the previous steps of the regeneration, the desired levels of carbon and sulfur can be achieved by adjusting the temperature and residence time of the catalyst in the unit. These conditions are chosen with consideration given to both maximizing the catalyst performance and the economic concerns of the vendor to maximize the regeneration rate.

The trend toward higher metal contents in modern, high performance hydrotreating and hydrocracking catalysts is of some concern because maintenance of a high degree of dispersion on the catalyst support becomes more difficult as the metals levels increase. More precise control of regeneration conditions is necessary to retain a high degree of metals dispersion. New technologies for regeneration tailored specifically to these types of catalyst are currently evolving.

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CATECHOL.

See HYDROQUINONE, RESORCINOL, AND CATECHOL.

CATHARTICS.

See GASTROINTESTINAL AGENTS.

CATIONIC DYES.

See DYES AND DYE INTERMEDIATES.

CAULKING COMPOSITIONS.

See SEALANTS.

CAUSTIC SODA.

See ALKALI AND CHLORINE PRODUCTS.

CELL CULTURE TECHNOLOGY

Cell culture processes, the *in vitro* growth of animal, insect, or plant cells on a large scale to manufacture biochemicals of commercial importance, have been used for some time for the manufacture of viral vaccines (see VACCINE TECHNOLOGY). Significant growth in this technology, primarily because of the advent of recombinant DNA methods (see GENETIC ENGINEERING) for the production of therapeutic proteins (qv) and hybridoma technology for production of monoclonal antibodies (see IMMUNOASSAY) occurred in the late 1980s and early 1990s. The need for cell culture technology stems mainly from the fact that bacteria do not have the capability to perform many of the post-translational modifications that most large proteins require for *in vivo* biological activity. These modifications include intracellular processing steps such as protein folding, disulfide linkages, glycosylation, and carboxylation.

Historically, large-scale cell culture technology traces its roots to the production of viral vaccines and other therapeutically important secreted products of human and primate cells such as those listed in Table 1. Most of these products were made by cells grown either in suspension or attached to microcarriers. Such cells were cultured in stirred tank reactors adapted from bacterial fermentation (qv) processes. The primary challenges in adapting microbial fermenters to the rigors of cell culture technology were reducing the risk of microbial contamination, modifying the agitation system to provide low shear agitation to the shear-sensitive mammalian cells, and providing adequate oxygenation under the low shear conditions mandated by the cells (see AERATION, BIOTECHNOLOGY).

Table 1. Historical Products of Cell Culture Technology

Product	Cell line	Process ^a	Year introduced	Reference
FMD ^b vaccine	baby hamster kidney	SC	1962	1
rabies vaccine	dog kidney	SM	1978	2
interferon	human namalwa	SC	1979	3
polio vaccine	monkey kidney	SM	1980	4

^a SC = suspension culture; SM = stirred microcarrier.

^b FMD = foot-and-mouth disease.

Although the number of cell culture-derived products on the market as of this writing is relatively small, there are several products in clinical trials and many more in development. Hybridomas, which are obtained by fusing a myeloma cell and lymphoid cells from mice immunized with a specific antigen, are used to produce monoclonal antibodies. Monoclonals have already found many uses in the diagnostic industry by virtue of extreme specificity of binding to an antigen of interest (see BIOSENSORS; MEDICAL DIAGNOSTIC REAGENTS). They have also found use for immunopurification and as therapeutics (see BIOPOLYMERS, ANALYTICAL TECHNIQUES; IMMUNOTHERAPEUTIC AGENTS). The quantities of monoclonals needed for diagnostics are relatively small and thus the scale of production is also small. Examples of uses of monoclonals in diagnostics are for detection of polypeptide hormones (qv), eg, human chorionic gonadatropin and human growth hormone; detection of tumor markers, such as alpha-fetoprotein; infectious diseases, such as chlamydia, herpes, and varicella; and cell surface antigens, eg, T-cells and leukemia typing.

Recombinant DNA technology has already provided several products of therapeutic interest from mammalian cells. Table 2 gives examples of products from mammalian cells, the use, and the technology used for production. Technology development for these products has centered around the differences in characteristics of mammalian versus microbial cells, notably, the shear sensitivity and susceptibility to contamination of the mammalian lines.

Table 2. Therapeutic Products from Mammalian Cells

Product	Company	Cell ^a	Process ^b	Therapeutic use
tissue plasminogen activator (tPa)	Genentech	CHO	SC	heart attacks
erythropoietin ^c	Amgen	CHO	ARB	anemia
factor VIII	Cutter Miles	CHO	SC	hemophilia
OKT-3	Ortho	hybridoma	MA	prevention of trans-plant rejection
centoxin	Centocor	hybridoma	SC	septic shock

^a CHO = Chinese hamster ovary.
^b SC = suspension culture; ARB = automated roller bottles; MA = mouse ascites.
^c CAS Registry Number is [11096-26-7].

Although the focus of this article is mainly on mammalian cells, the technologies described herein also apply in principle to insect and plant cells.

Characteristics of Mammalian Cells

Environmental Conditions. Mammalian cells *in vivo* are maintained in a carefully balanced homeostatic environment and thus have evolved to require fairly stringent environmental conditions. These cells differ significantly from bacterial cells in that they lack a rigid cell wall and are hence much more shear sensitive. Many animal cells are also attachment dependent, needing a surface to grow on. Many of the cell culture technologies provide the low shear, high surface area environment needed for the mammalian cells. Another approach, however, is to adapt cells to suspension culture and select cells that are less shear sensitive permitting the use of fermentation technology for the culture of animal cells. The optimum environmental parameters depend on cell type and are specific to cell type. Typical ranges for some of these parameters are listed in Table 3.

Table 3. Environmental Parameters for Mammalian Cell Cultivation

Parameter	Range	Typical value
pH	6.6–7.6	7
temperature, °C	33–39	37
dissolved oxygen, Pa ^a	0.7–40	10
osmolarity, mOsm/kg ^b	280–360	300
dissolved CO ₂ , Pa ^a	0.9–20	7
tolerable shear rate, s ^{–1}	0–3000	1500

^a To convert Pa to mm Hg, multiply by 7.5.
^b mOsm = milliosmolar or milliosmole where an osmole equals a mole of solute divided by the number of ions formed per molecule of the soluble, ie, one mole of sodium chloride is equivalent to two osmoles of sodium chloride and 1 M NaCl = 2 Osm NaCl.

Nutritional Requirements. The nutrient requirements of mammalian cells are many, varied, and complex. In addition to typical metabolic requirements such as sugars, amino acids (qv), vitamins (qv), and minerals, cells also need growth factors and other proteins. Some of the proteins are not consumed, but play a catalytic role in the cell growth process. Historically, fetal calf serum of 1–20 vol % of the medium has been used as a rich source of all these complex protein requirements. However, the composition of serum varies from lot to lot, introducing significant variability in manufacture of products from the mammalian cells.

Serum is expensive, the 1992 price was \$400/L, and supply depends on cattle supply. Use of this serum also poses significant difficulties in validating processes for absence of viral contamination. Hence, a goal in cell culture technology is to develop serum-free media for cell culture. Much work has gone into developing serum-free media and a sizable portion of cell culture research is devoted to this project. A detailed discussion of serum-free media development is available (5).

Several generic media formulations have been developed for growth and cultivation of mammalian cells and are commercially available. Each contains amino acids, inorganic salts for providing the right osmolarity, essential minerals, and buffering capacity; vitamins, and energy sources such as glucose. Whereas mixtures of the different formulations are often used to optimize growth and productivity of cell lines, many of the basal media need to be supplemented with serum or other appropriate proteins for promoting cell growth. Some of the more commonly used media formulations include: minimum essential medium (MEM) for a broad spectrum of mammalian cells; basal media eagle (BME) for diploid or primary mammalian cells; Dulbecco's modified eagle media (DMEM) for a broad spectrum of cells; CMRL media for Earle's "L" cells and monkey kidney cells; Fischer's media for murine leukemic cells; Iscove's modified Dulbecco's media (IMDM) for rapidly proliferating high density cell cultures; McCoy's media for human lymphocytes; Ham's F10 and F12 for Chinese hamster ovary cells and other mammalian cells; and RPMI 1630/1640 for suspension cells and human leukemic cells. These media are available from Gibco Laboratories (Grand Island, New York), Irvine Scientific (Santa Ana, California), Sigma Chemical Co. (St. Louis, Missouri), Hyclone Laboratories (Logan, Utah), and JRH (Lenexa, Kansas) among others.

Another essential nutrient not supplied with the media is oxygen. The oxygen consumption rate of mammalian cell cultures is much lower than that of bacterial ones because cell densities are much lower than those achieved in bacterial cultures. The oxygen consumption rate varies from cell line to cell line, but the range has been reported to be as wide as 0.05–0.5 mmol/(10⁹ cells·h) (6). Hence, designing oxygenation systems for mammalian cells is a function of the cells being used. Use of the worst case scenario may lead to costly overdesign. This is especially so if silicone tube oxygenators are being considered. Direct sparging in the reactor to accomplish oxygen transfer often leads to cell damage unless protective agents, such as pluronic polyols, are used (7). However, as long as the pluronic is nontoxic to the cells and is compatible with downstream processing steps, this use is probably the most efficient route to oxygenating cell culture systems. Most cell lines also require a small amount of dissolved carbon dioxide for growth, especially at low cell densities.

Kinetics of Cell Growth and Product Formation. Mammalian cells grow at a much slower rate than bacterial and yeast cells (see YEASTS). The maximum specific growth rates for mammalian cells range from 0.01 to 0.05 h^{–1}, corresponding to cell doubling times of 14 to 70 hours depending on the cell line and environmental conditions. Most primary cell lines are anchorage dependent and need a surface to grow on. They are also contact inhibited, ie, they stop growing once the surface is confluent. Alternatively, most of the cell lines used industrially for recombinant products and monoclonal antibodies are not attachment dependent. For example Chinese hamster ovary (CHO) cells are commonly used as host cells for recombinant products. These cells are transformed by tumor viruses and do not require a surface to grow on. They do, however, prefer to grow on surfaces and requirement for serum factors diminishes significantly when they are attached to surfaces. Thus CHO cells can be cultured for several weeks in protein-free media if grown on microcarriers, whereas they require serum proteins such as fetuin to grow in suspension. Most hybridomas used for making monoclonal antibodies are attachment independent, grow in suspension, and have minimal requirement for serum proteins. It is necessary to adapt these cells to serum-free media for several days before they start growing well in these media.

Cell growth kinetics of mammalian cells can be described by the typical lag, exponential growth, then stationary and death phases. The exponential phase may be described adequately by a Monod type of kinetic model when the growth rate is much larger than the death rate. At low growth rates, it is necessary to include cell death kinetics to account for the lower viability and to predict the cell viability. Toward the end of the exponential culture, cells are also subject to growth inhibition from metabolic by-products such as lactate and ammonia. Hence, for continuous processes, a comprehensive model should contain terms for cell growth, based on the limiting substrate concentration, cell death, and inhibition kinetics.

Product formation kinetics in mammalian cells has been studied extensively for hybridomas. Most monoclonal antibodies are produced at an enhanced rate during the G_0 phase of the cell cycle (8–10). A model for antibody production based on this cell cycle dependence and traditional Monod kinetics for cell growth has been proposed (11). However, it is not clear if this cell cycle dependence carries over to recombinant CHO cells. In fact it has been reported that dihydrofolate reductase, the gene for which is co-amplified with the gene for the recombinant protein in CHO cells, synthesis is associated with the S phase of the cell cycle (12). Hence it is possible that the product formation kinetics in recombinant CHO cells is different from that of hybridomas.

Cell Culture Processes

A wide variety of mammalian cells are used in industrial practice and to accommodate the diversity, a variety of cell culture technologies have evolved depending on the cell line and product characteristics.

Batch Suspension Culture The batch suspension culture is perhaps the simplest technology available. It is adapted from traditional bacterial fermentation (qv) technology by changing the impellers to low shear marine propeller type, thus reducing the shear forces to which cells are subjected. Oxygenation is achieved either by direct sparging, if the cells are not subject to damage by bursting bubbles or are protected by surface-active agents such as pluronic polyols, or by membrane oxygenation where gas-permeable tubing is inserted into the fermentor.

Most hybridomas can be grown in batch suspension culture. Recombinant CHO cells can also be adapted for growth in suspension. However, CHO cells often require serum or expensive serum proteins to grow in this manner. The applicability of this process hinges on whether an inexpensive serum-free medium can be developed for the cells in question and whether the proteins used for serum-free media development, eg, bovine serum albumin [9048-46-8] can be effectively separated from the product during downstream processing. Viral vaccines are often produced in suspension culture reactors because the product is isolated from the cells and presence of serum is not a hindrance to purification. For example, FMD vaccine is produced in 3000-L batch suspension culture reactors (13). Genentech produces tPA in 10,000-L batch fermenters using recombinant CHO cells. It is believed that these cells are grown to high densities in serum-containing media, then shifted to a low protein production medium for harvesting the secreted product. Batch suspension culture is also used for large-scale production of monoclonal antibodies. Celltech has scaled up airlift suspension culture reactors to 2000-L scale for the production of monoclonals (14).

A batch suspension culture reactor consists of a stirred tank typically having a height to diameter ratio of 1:1 to 3:1, fitted with a low shear impeller. The tank has a hemispherical bottom to avoid stagnant zones, because agitation level is very low, and the agitator shaft is either magnetically coupled to the motor or is coupled with a double mechanical seal to protect the culture from contaminating microorganisms. The vessel is pressure rated for in-place steam sterilization. Medium is filtered into the fermentor through a 0.1 micrometer absolute filter. Inoculum is added via a steam sterilized connection from the inoculum fermentor. The seed fermentor is typically one-tenth the size of the production fermentor. Hence, for large-scale production purposes, a long inoculum train is required. Oxygenation may be effected by either direct sparging into the fermentor or by using a coil of gas permeable tubing, either silicone or microporous Teflon tubing. The vessel is fitted with temperature, dissolved oxygen, and pH probes. pH is controlled by addition of carbon dioxide (qv) to lower the pH and a suitable base, eg, dilute NaOH or NaHCO_3 , to raise it. Dissolved oxygen is controlled by addition of air and or pure oxygen. Insulated jackets are used for controlling the temperature. The vessel is manufactured from 316 L stainless steel and polished to a high degree, typically 240 grit followed by electropolishing, for ease of cleaning. Other materials used for seals, etc, are restricted to medical-grade silicone, Teflon, Viton, and borosilicate glass to ensure that toxic materials do not leach into the culture and affect the cells.

Figure 1 shows a schematic of a typical cell culture manufacturing facility using batch suspension culture. The downstream processing of harvest from the fermentor usually consists of a clarification step, either a centrifuge or a microfilter, followed by a concentration diafiltration step using a tangential flow ultrafiltration membrane of an appropriate molecular weight cutoff. The concentrated protein is further purified by a series of chromatography (qv) steps. The downstream processing steps are usually similar regardless of the cell culture technology being used.

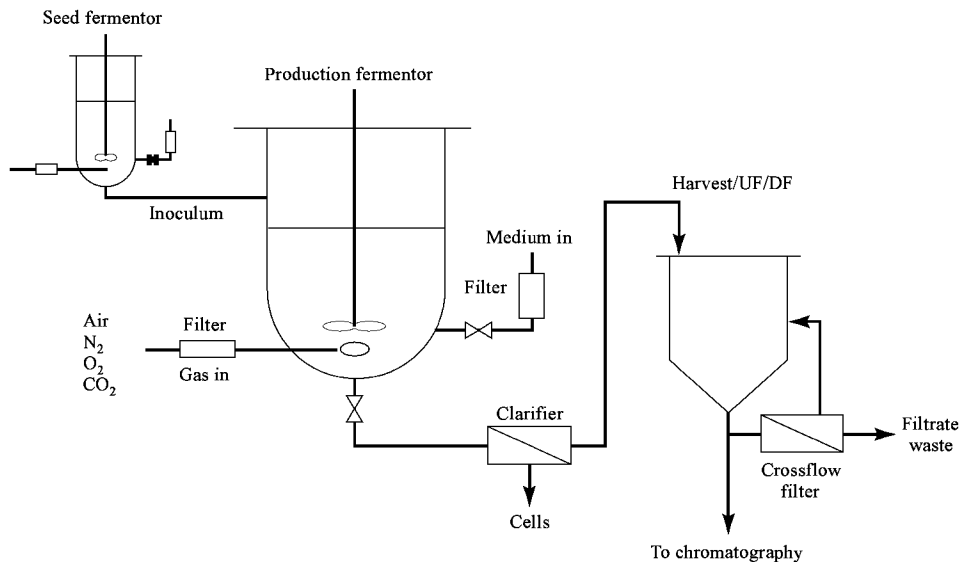


Fig. 1. Schematic of a process for batch suspension culture of mammalian cells, where UF is ultrafiltration and DF is diafiltration.

Batch suspension culture has many inherent advantages. It is relatively simple to operate and scale up and less susceptible to microbial contamination. The homogeneous nature of the process makes process control (qv) and optimization easier, and from a regulatory point of view, it is the easiest to define and validate. This is therefore the process of choice if the cells can be grown in suspension in a relatively inexpensive medium. A disadvantage of the process is that labile products may degrade during the long batch periods, especially because of the presence of proteases released by lysed cells toward the end of the process. For such products, a continuous process having low reactor residence times may be more suitable.

Batch Microcarrier Process. For attachment dependent cells, the batch microcarrier process is the equivalent of the batch suspension process except for the fact that cells are attached to microcarriers. Cells attached on the surface of microcarriers are far more sensitive to shear forces than suspension cells because microcarriers are much larger than suspended cells. The damage to cells is theorized to be caused primarily by turbulent eddies when the eddy size becomes smaller than the particle size of microcarriers. Another mechanism for cell damage, especially at high bead concentration, is the bead to bead collision frequency. These mechanisms of cell damage in microcarrier cultures are discussed in the literature (15,16). Because of this limitation on agitation power input, agitator design is of great importance in microcarrier reactors. High efficiency impellers, which maximize flow and

minimize shear, are utilized. The shear effects mentioned here are applicable to solid microcarriers where the cells are attached to the surface. Most recently, some macroporous carriers have been introduced that prevent the shear damage by providing attachment surfaces on the internal pores of the carriers. However, the attachment rate on such microcarriers is slower than that on solid microcarriers. This makes the porous microcarriers more suitable for long-term perfusion cultures.

Many microcarriers are now available commercially for mammalian cell culture. The choice of microcarrier depends to some extent on the cell line being used and whether a batch or continuous process is being contemplated. Table 4 lists some of the microcarriers commercially available. The Cytodex family of beads is probably the most widely used. Cytodex 2 is recommended for cells having fibroblastlike morphology; Cytodex 3 is recommended for cells having an epithelial-like morphology. In long-term serum-free cultures, Cytodex 2 cells tend to retain cells longer than Cytodex 3, whereas the latter is useful when available inoculum density is low. In some cases, productivity is affected by the surface characteristics. For example, some cells have higher productivity on negatively charged polystyrene, eg, Biosilon, than the positively charged dextran. In designing a microcarrier process,, it is recommended that a quick screening experiment be conducted to assess the suitability of the microcarriers available. A more extensive review of various types of commercial and noncommercial microcarriers and their applications is available (17).

Table 4. Microcarriers for Stirred Tank Reactors

Trade name	Manufacturer	Diameter, μm	Characteristics
Cytodex 1	Pharmacia, Sweden	147–248	dextran, high positive charge
Cytodex 2	Pharmacia, Sweden	135–200	dextran, positive charge
Cytodex 3	Pharmacia, Sweden	141–211	collagen-coated dextran
Biosilon	Nunc, Denmark	160–300	polystyrene, negative charge
Cultispher	Hyclone, United States	170–270	gelatin, macroporous
Bioglas	Solo Hill, United States	90–150	glass-coated plastic
Bioplas	Solo Hill, United States	90–150	cross-linked polystyrene

In addition to attachment dependent cells, a batch microcarrier process may also be used for other cells that can grow in the attached mode because it allows the use of totally protein-free media. Many cells can survive for long periods of time in completely protein-free medium if attached to a surface. However, microcarrier reactors face several practical difficulties. First, if the cells are attachment dependent, generating sufficient inoculum for large-scale reactors involves trypsinization of microcarriers from a smaller reactor and reattachment in the larger reactor. The exposure to trypsin [9002-07-7] has to be controlled carefully in order to minimize cell damage. Second, the switch to a protein-free medium entails draining the reactor and refilling with fresh medium, requiring settling of the beads for long periods of time, especially in large-scale reactors. During this time, the cells may be deprived of oxygen and other nutrients and may be affected adversely. Hence batch microcarrier processes are suitable for vaccine manufacture where presence of serum may not be a hindrance. Finally, the low shear requirements make oxygenation much more difficult than in suspension culture. Gas sparging tends to carry all the microcarriers into the foam layer because the beads tend to adhere to the bubbles as they rise through the liquid. One approach to solving this problem is to aerate the liquid in a rotating or vibrating cage, separating the microcarriers from the bubbles. The movement of the cage prevents the cage from getting clogged, especially in a perfusion system, with cells and microcarriers. Alternatively, gas permeable tubing may be used. Many fermentor manufacturers now offer caged aeration and perfusion systems as an option for cell culture fermentors. These include Sulzer MBR (Switzerland), Applikon (The Netherlands), New Brunswick Scientific (United States), Biolafitte (France), B. Braun (Germany United States), and Chemap (Switzerland). B. Braun and Bioengineering (Switzerland) also offer silicone membrane oxygenation as an option. Membranteknik (Switzerland) offers silicone membrane oxygenating systems to retrofit existing fermentors for enhancing oxygenating capabilities. A good overview of microcarrier culture technology and an in-depth discussion of design issues and applications is available (18).

Microcarrier Perfusion Systems. Microcarriers may also be used in a continuous perfusion mode. In the perfusion mode, the reactor is constantly fed with fresh, sterile medium and product is harvested from the reactor at an equal rate. Perfusion systems have the advantage that the same cells can be maintained in a productive mode for several days, thus reducing costly downtime and the cost of expensive growth medium. Once the cells attach to the carriers and become confluent, they can be maintained in a productive mode in protein-free medium for several days or, depending on the cell line, for several months. High density perfusion systems are also useful for labile products, because low residence time in the reactor minimizes the exposure of the product to degradative enzymes and conditions. Continuous systems allow steady-state operation, which makes process control and process optimization easier. Continuous processes suffer two principal drawbacks. First, the risk of contamination is higher because of the increased complexity of the process. Additionally, contamination is much more costly for a continuous process than a batch process because the magnitude of product and labor loss is much higher. Second, if the cell line is subject to genetic instability, the reactor may lose productivity over a long period because of slow overgrowth of nonproducing cells. Further, it is harder to define a batch for regulatory purposes when the product is being made by a slowly changing population of cells, making validation of the process that much more difficult.

Figure 2 shows a typical microcarrier perfusion system utilizing a rotating screen to separate the microcarriers from the harvest liquid. Oxygenation using silicone tubing in the form of a helical coil is shown. Oxygenation can also be accomplished by sparging gas within this cage. Either method eliminates the possibility of damage to the cells from gas bubbles. The medium and harvest tanks are usually sized to hold at least three days worth of medium. Peristaltic or steam sterilizable diaphragm metering pumps are commonly used for pumping the medium and harvest. Steam sterilizable connections are used to maintain sterility during medium feed and harvest operations. Although the screen is shown as mounted on the agitation shaft, it is possible to attach the screen to a separate shaft driven by a second motor. The latter system has the advantage that the rotational speed of the screen can be optimized for microcarrier rejection without affecting the mixing and shear characteristics of the agitator. Other methods for retaining microcarriers within the reactor include settling towers, based on gravity settling of microcarriers, and "self-cleaning" static screens (19). In long-term continuous operation, cells tend to clump up and detach from nonporous microcarriers. For this reason, the macroporous carriers may be more suitable for long-term perfusion cultures.

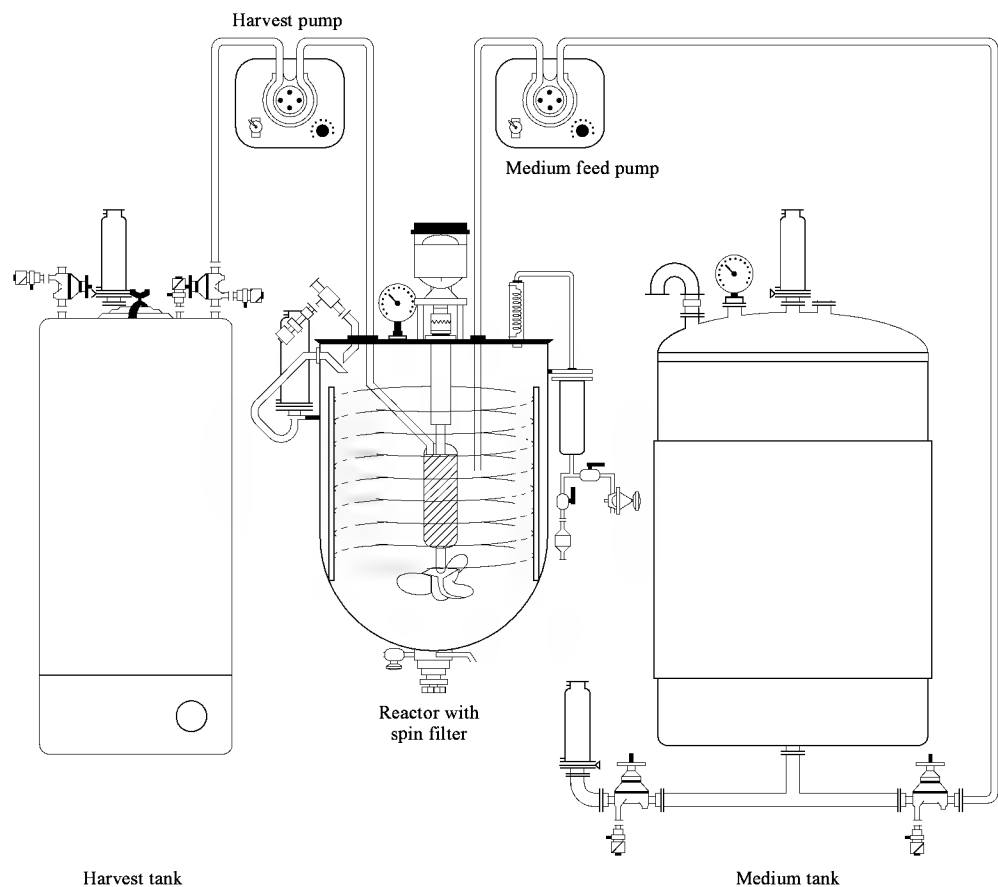


Fig. 2. Schematic of a process for microcarrier perfusion culture using a spin filter device.

Process design for microcarrier processes involves determination of the surface area of carriers required to accomplish the production in a given time. This can be translated from small-scale T-flask culture experiments. There is a practical limit to the surface area per unit volume that can be accommodated in a reactor. For example, for carriers having an average diameter of 150 μm , 30,000 cm^2/L is a reasonable limit. Beyond this limit the collision severity becomes a factor in cell damage. The reactor volume is determined based on these numbers and provision is made for the necessary oxygen transfer depending on the specific oxygen transfer rate of the cells. The procedures used for designing and scaling up microcarrier reactors have been described (20).

Fluidized-Bed Systems. Another approach to obviating the shear damage problem and to provide sufficient oxygenation to a high density cell culture system is to employ a fluidized-bed system utilizing macroporous microcarriers. Verax (Lebanon, New Hampshire) has developed a system to culture cells at high densities in a fluidized-bed reactor where the carriers are fluidized by the recirculating medium which is continuously oxygenated by a membrane gas exchanger outside the reactor. The cells are immobilized in macroporous carriers made of collagen. Fresh medium is continuously added to this loop and equivalent amount of product harvested at the same time. The porous carriers are weighted to allow high enough recirculation rates through the bed so that sufficient oxygen can be provided to all the cells. pH, dissolved oxygen, and temperature sensors are also located in the recirculation loop and these parameters are controlled via a computer-based control system. A schematic of this process is shown in Figure 3; examples of usage are available (21).

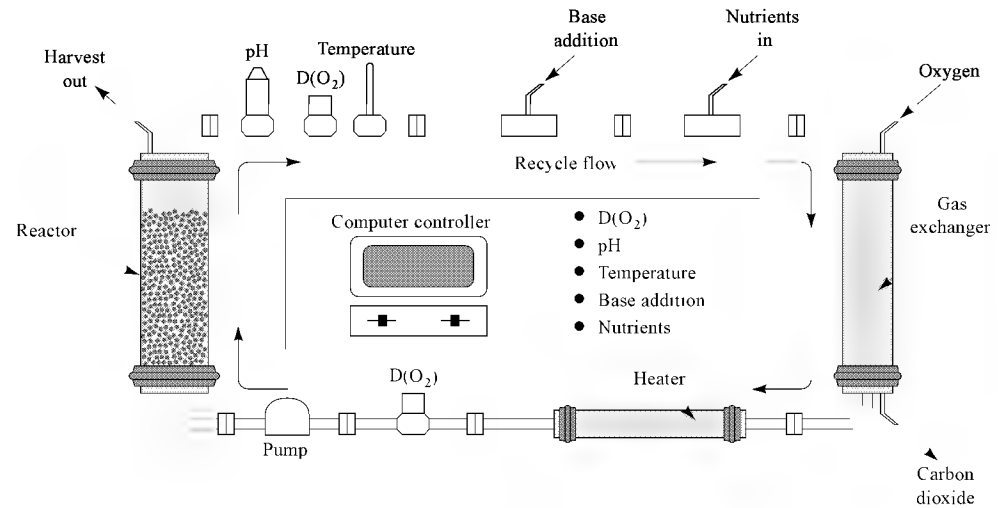


Fig. 3. Schematic of a fluidized-bed process for mammalian cell culture where $\text{D}(\text{O}_2)$ = dissolved oxygen.

Courtesy of Verax Corp.

Advantages of this system include: both anchorage dependent and independent cells can be cultured in this system without the danger of adverse shear effects; most of the control and instrumentation is located in the external loop and it is therefore possible to build in redundant loops and increase the reliability of the process; high (up to 3×10^8 cells/mL of matrix) cell densities allow short (2–5 h) residence times, which is helpful for labile proteins that are subject to degradation. This system also has the advantages of high cell density cultures while providing a relatively homogeneous environment for the cells. On the other hand the system has some limitations. Because of the limit on recirculation flow rate, set by the specific gravity of the matrix, the depth of the fluidized bed is limited to about 1.5 m. Scale-up beyond this is possible only by increasing bed diameter. Moreover, an oxygen-transfer gradient is imposed on the bed because of the rapid rate of oxygen consumption prohibiting the precise optimization of dissolved oxygen. Finally, as with any continuous system, the complexity of the system makes it harder to set up, although it is easier to operate, and the costs associated with contamination

can be very high.

Another version of a fluidized-bed reactor has been introduced by Vogelbusch (Austria). This reactor has an internal recirculation loop set up by means of a high flow impeller. The system utilizes porous glass beads for immobilizing the cells. However, glass beads may not work with all types of cells.

Fixed-Bed Reactors. A fixed-bed reactor has been developed by Charles River Biotechnical Services (Wilmington, Massachusetts) for the culture of both anchorage dependent and independent cells. A ceramic matrix having multiple internal channels through which the recirculating medium flows is used. A smooth matrix is employed to immobilize attachment dependent cells whereas another matrix having surface pores serves as the immobilization support for other cells. The process concept is similar to that of the recirculation loop for the fluidized-bed system. Figure 4 shows a schematic of this system. Because the bed is fixed, recirculating flux rates can be higher than in fluidized systems.

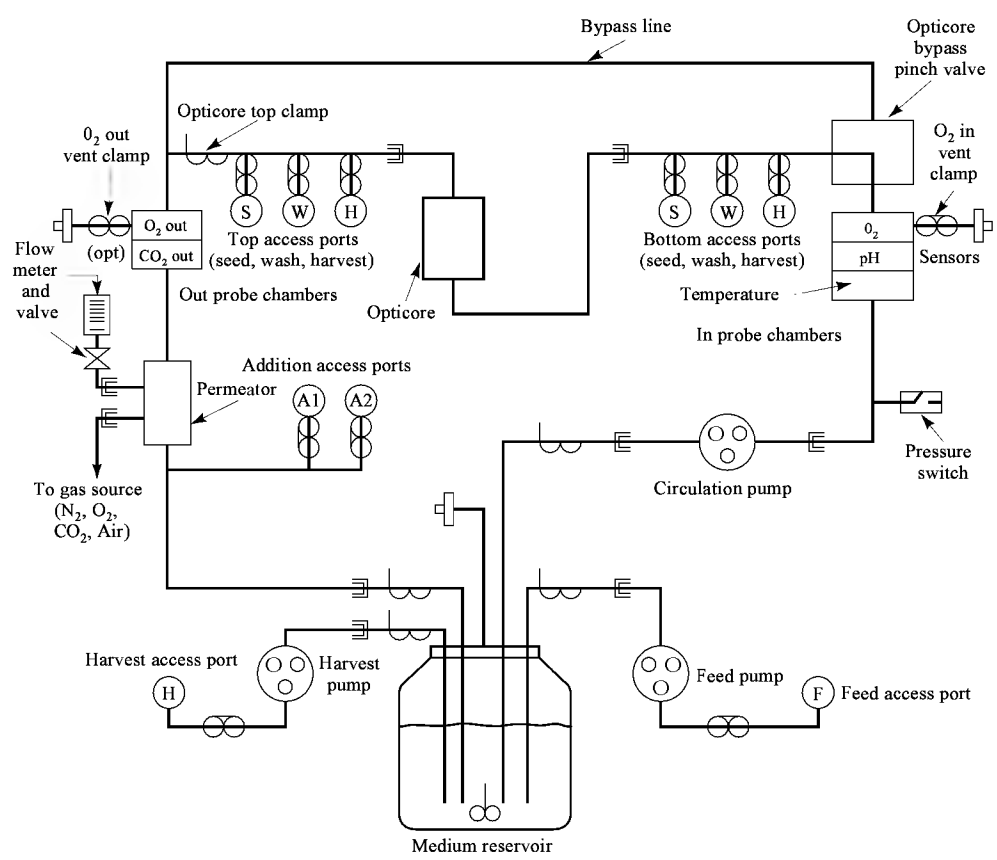


Fig. 4. Schematic of a fixed-bed process for culturing mammalian cell using ceramic matrix.

Courtesy of Charles River Biotechnical Services.

Scale-up in fixed-bed reactors is limited by the maximum size of the matrix that can be manufactured as a monolith. Hence, this system is applicable for small- to medium-scale production of antibodies and other proteins, usually for the diagnostic market. This system has been described in greater detail in the literature (22).

Another type of fixed-bed system is the hollow-fiber reactor. A hollow-fiber device consists of a bundle of hollow fibers, usually made of hollow anisotropic plastic fibers that allow diffusion of molecules smaller than a specified molecular weight cut-off, potted at both ends of a plastic shell (see HOLLOW FIBER MEMBRANES). The cells are immobilized in the extra capillary space (ecs) of the hollow fibers and the medium recirculates through the lumen of the fibers entering and exiting via headers at either end of the reactor. The cells are held in a static mode and grow to high tissuelike density in the ecs. The medium access to the cells is via diffusion and Starling flow. Thus shear forces on the cells are minimal. This system is especially suitable for cells that are extremely sensitive to shear induced injury. Another advantage is that the fibers can be specified such that the product, often a high molecular weight protein, can be retained within the ecs, while medium components and metabolic by-products can diffuse through. This arrangement allows for *in situ* concentration of the product to very high levels. Similarly, serum usage can be minimized by entrapping the high molecular weight protein components of serum in the ecs and using protein-free medium for perfusion.

Scale-up of this system is limited by the size limitation on hollow-fiber manufacturing. This system is also more suitable for the diagnostic markets where quantities of protein required are relatively low. A disadvantage of the system is that nutrient gradients are set up in the ecs leading to a nonhomogeneous environment making process control difficult. Endotronics has devised a way of solving this problem by pressure induced flow through the ecs (23). However, this increases the complexity of the system. Hollow-fiber devices are available through many vendors including Endotronics (Coon Rapids, Minnesota), Microgon (Laguna Hills, California), Unisyn Fibertec (San Diego, California), and Amicon (Beverly, Massachusetts). Some offer complete cell culture systems (Endotronics, Unisyn Fibertec, Amicon); others sell only the hollow-fiber device and leave the system design to the user.

Cell Recycle Systems. A variation of suspension culture reactors is a system where the cell concentration is increased by perfusing medium through the reactor continuously while retaining the cells in the reactor by means of a tangential flow filter. The tangential flow filter can be either a plate and frame filter, eg, the Prostack manufactured by Millipore, or a hollow-fiber device. Figure 5 gives an example of one such system. Cells are continuously recycled from the fermentor through a tangential flow filter. The filtrate removed from the filter is replaced by fresh medium from the medium tank. A small fraction of cells are either continuously or periodically purged from the reactor to maintain cell viability at a high level. This type of reactor provides the benefits of a high cell density system and maintains a homogeneous environment for the cells. A shortcoming of the system is that its applicability is limited to anchorage independent cells. It is also fairly complex to set up because of the external recirculation loop involved. It is possible to internalize the cell recycle by using an appropriately sized spin filter device like the one shown in Figure 2. However, such systems are prone to clogging by the cells after a few days of operation. These systems can be effectively utilized when there is a need to increase the capacity of existing stirred tank fermentors.

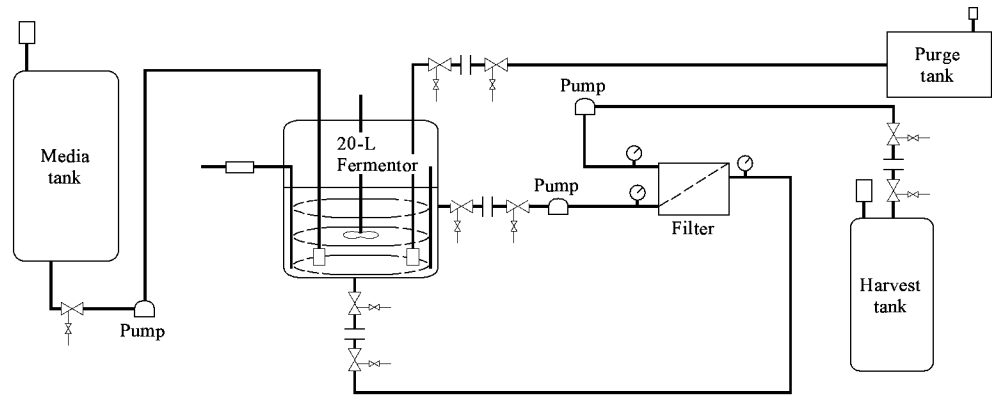


Fig. 5. A suspension perfusion culture process having cell recycle. System employed at Amgen using CHO cells for production of a recombinant protein.

Other Systems. There are several other technologies utilized for specific purposes that do not fall into any of the above categories. For example, erythropoietin is produced in an automated roller bottle plant where cells are grown on the surface of roller bottles in a growth medium. Cells are then shifted to a serum-free production medium for harvesting. All operations are carried out aseptically in a clean room environment by an automated machine providing a high degree of reliability and consistency. Although roller bottles are often considered to be obsolete because of the labor and space intensive nature of the process, automation makes them a viable process for products where the volume requirements are not very high. The Technology Partnership (Cambridge, England) offers robotic systems for the production of cell culture-derived products using roller bottles and T-flasks. Other systems attempt to scale up existing T-flask processes linearly by increasing the available surface area in a compact space and providing methods for media addition and harvest removal. Examples of such systems include the cell factory marketed by Nunc (Denmark) and the cell cube marketed by Costar (Cambridge, Massachusetts). Both systems are suitable for small-scale manufacturing, using attachment dependent cells. They have the advantage of assuring the fidelity of the process as it is scaled up from T-flasks.

Economic Aspects

As of early 1992, the market for cell culture-derived products approached \$1 billion per year. The market is expected to grow substantially throughout the 1990s. Cell culture products include erythropoietin, 1991 sales of approximately \$400 million, for the treatment of anemia associated with kidney dialysis, and tissue plasminogen activator, 1991 sales approximately \$200 million, for treating heart attack victims with blocked arteries (see *CARDIOVASCULAR AGENTS*).

Process Economics. Relative economics of various cell culture processes depend heavily on the performance of the cell line in a system and on the cost of raw materials, particularly the medium. Models are usually developed for the various processes using productivity data obtained from small-scale experiments (see *PILOT AND MICROPLANTS*). Often, for high value products, the process which ensures the shortest time to market may be the process of choice because of other economic criteria. This is especially true for pharmaceuticals (qv). Reliability concerns also often outweigh economic considerations in choosing a process for a high value product.

Continuous processes have lower labor costs but have higher failure risk. Batch processes can be started back up in a shorter period of time than can a complex continuous process. Batch processes are easier to take through the regulatory process than are continuous processes. Thus batch processes are often chosen for mammalian cell culture systems, even though continuous processes can offer significant cost advantages. Cell culture costs constitute only a small (10–30%) fraction of the overall cost of making a product.

Regulations and Standards

Most of the products derived from cell culture technologies are for therapeutic or diagnostic applications and manufacture is regulated by the federal government through the Food and Drug Administration (FDA). The FDA requires that all drugs be manufactured in compliance with current Good Manufacturing Practices (cGMPs). Guidelines for cGMPs are provided through the *Code of Federal Regulations* (CFR) Title 21. Essentially, cGMPs require that all process steps and products be defined in a quantitative manner by the manufacturer, ie, specifications for all important processes must be developed and methods for testing and validating those steps must be identified. The National Institutes of Health have issued guidelines for safe experimentation using recombinant and mammalian cell lines (24).

The biotechnology (qv) industry has no formal standards for equipment manufacture and quality control as of this writing. The American Society of Mechanical Engineers (ASME) set up a task force in 1989, for developing relevant standards for biotechnology equipment.

Safety Considerations

The fact that cell culture-derived products are often injected into humans as therapeutic agents makes it imperative that there be no component in the final product that can pose a potential health risk to the patient. Health risks can be introduced into a product from many sources including: the cells themselves; raw materials, such as serum, media components, etc; materials used in purification, eg, antibodies; and external contamination. For a therapeutic product such risk factors are identified at the outset and ways of reducing them to acceptable levels are designed into the process. Before a product is released by the FDA the manufacturer has to demonstrate this risk reduction by rigorous validation of the process.

Some of the cells used in manufacturing are continuous or "immortal." Many of these have been shown to be tumorigenic in immunosuppressed animals. The cells also contain endogenous materials such as retroviruses and nucleic acids (qv), both of which can induce tumorigenesis, and immunogenic foreign proteins. Serum used in media can also introduce adventitious agents such as viruses and mycoplasma into the product. Other process chemicals, including cleaning agents, are low molecular-weight compounds that may be hazardous as well. Purification chemicals, such as monoclonals used for affinity purification, can be immunogenic to humans. Some of the potential health risks in mammalian cell culture processes and the methods used for risk reduction include:

cells	microfiltration
retroviruses	irradiation, sonication, heat, solvents, etc
nucleic acids	chromatography
cellular proteins	chromatography, ultrafiltration
bacterial contamination	microfiltration
process chemicals	diafiltration with appropriate buffers
serum proteins	affinity ion-exchange chromatography

Most of these methods are commonly employed in the downstream processing of the desired cell culture technology product. Hence, most of the time it is only necessary to demonstrate that the designed process is reducing the putative risk factors to acceptable levels. Validation methods employed for risk reduction are discussed in the literature (25).

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CELLOPHANE.

See FILM AND SHEETING MATERIALS.

CELLS, ELECTRIC.

See BATTERIES.

CELLS, HIGH TEMPERATURE.

See BATTERIES.

CELLULOSE

Cellulose [9004-34-6], characterized by Anselme Payen in 1838, is the main component of higher plant cell walls. It is also formed by some algae, fungi, bacteria, and a group of invertebrate marine animals, the tunicates. It is even produced by humans suffering from the rare disease, scleroderma. The secondary cell walls of cotton fibers are almost pure (about 94^o %) cellulose. Cellulose from other plants, such as mature wood, is encrusted in as much as 36^o % lignin, a three-dimensional polymer of several aromatic compounds. About 7.5 × 10¹⁰ t of cellulose grow and disappear each year, establishing it as the most abundant regenerated organic material on earth.

Natural cellulosic materials such as grass are eaten by grazing animals, and various species build nests or dens with wood. Cellulose in wood (qv) or in animal manure, along with lignin (qv), serves directly as fuel while scientists strive to develop efficient conversion of cellulose to alcohol and other fuels. After minimal processing of natural cellulosic materials, they are used as lumber and as textiles based on cotton (qv), jute, ramie, flax (linen), and hemp (see FIBERS, VEGETABLE). After industrial treatment, with and without chemical derivatization, cellulose is made into diverse products including paper, membranes, explosives, textiles (rayon and cellulose acetate), and dietary fiber (see FIBERS, CELLULOSE ESTERS; FIBERS, REGENERATED CELLULOSICS). The U.S. consumption of paper (qv) and board products made from wood pulp in 1987 was 312 kg per person, an increase of more than 45 kg since 1974 (1).

Native cellulose is fibrous and rather insoluble. Its fibers are relatively strong, having breaking strengths of up to 1 GN m² (145,000 psi) and moduli of elasticity ranging from 70 to 137 GN m² (10–20 × 10⁶ psi) (2). The strength and insolubility result because cellulose is an extended, ribbonlike molecule that forms both hydrogen bonds and hydrophobic attractions. Because of the chemical and biochemical stability of cellulose and its combination with lignin, some trees live thousands of years; some bristlecone pines (*Pinus longaeva* (arista) in Colorado are more than 5000 years old.

In the secondary cell wall of plants, cellulose molecules are unbranched chains of up to 17,000 1,4 linked β-D-glucose [492-61-5] residues (Fig. 1), but shorter chains occur under other circumstances. In industrial terminology, α-cellulose includes these molecules although some insoluble hemicelluloses [9034-32-6] may also be present. Hemicelluloses (qv), which occur along with cellulose in plant cell walls, are polysaccharides such as xyloglucan, glucomannan, and acetylated glucurono xylan. Other hemicelluloses are natural derivatives of cellulose itself, with side chains of xylose, and galactose and fucose in some cases. Holocellulose is an industrial word for delignified cellulose that still contains the hemicellulose. In the older nomenclature, β- and γ-cellulose are fractions of hemicellulose and degraded cellulose that are insoluble and soluble, respectively, after their alkaline solution is neutralized. All of this industrial terminology predates explicit knowledge of the chemical and physical structures of these polysaccharides. The word cellulose means β-1,4-D-glucan, regardless of source.

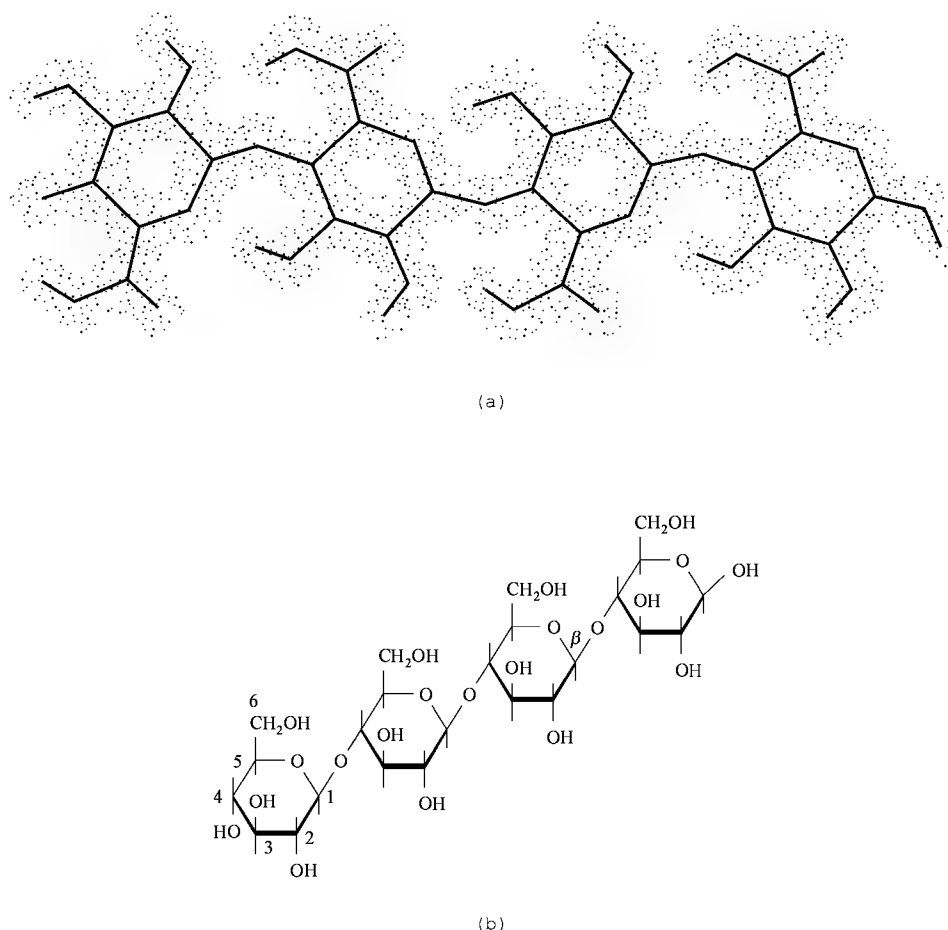


Fig. 1. A segment of a cellulose chain composed of four β -D-glucopyranose residues (cellotetraose), showing (a) the chemical bonds and electron clouds around the atoms. The molecule has the twofold helical conformation typical of many models of crystalline cellulose. (b) The (Haworth) structural formula shows the β -1,4 linkages between glucose units.

Because of the importance of cellulose and the difficulty in unraveling its secrets, several societies (Cellucon, American Chemical Society, and TAPPI) are dedicated to cellulose, lignin, and related molecules, as is at least one journal that is abstracted by *Chemical Abstracts* (3). The length of the proceedings of the Tenth Cellulose Conference (1638 pages) (4) indicates the vitality and interest in this subject, but research results are published in many other journals as well. There are also several recent books on cellulose (5–9). Reference 10 is a comprehensive review and is recommended especially for the historical review of proof of chemical structure, one of the milestones in organic chemistry.

Sources

Cellulose for industrial conversion comes from wood and scores of minor sources such as bagasse, the stalks of sugar cane from which the juice has been pressed. Bagasse is burned for fuel in Hawaii to provide as much as one-third of its electrical power (11). Although most papers and rayons are made from wood pulp, cotton is sometimes an ingredient as well. The importance of cellulose recycling is increasing, especially for paper products. On a more biological level, the majority of cellulose is in plant secondary cell walls, where it is usually the principal material. Primary cell walls have a lower cellulose content, are less crystalline, and the molecules have a lower molecular weight. Some cellulose comes from the hairs on seeds, eg, cotton, kapok, and milkweed. The bast fibers such as hemp, ramie (a perennial Asian nettle), linen, and jute are obtained from the stems of plants.

A commercial bacterial cellulose product (Cellulon) was recently introduced by Weyerhaeuser (12). The fiber is produced by an aerobic fermentation of glucose from corn syrup in an agitated fermentor (13,14). Because of a small particle diameter (10 μm), it has a surface area 300 times greater than normal wood cellulose, and gives a smooth mouthfeel to formulations in which it is included. Cellulon has an unusual level of water binding and works with other viscosity builders to improve their effectiveness. It is anticipated that it will achieve GRAS status, and is neutral in sensory quality; microcrystalline cellulose has similar attributes.

Bacterial cellulose is of research interest because it forms tangled extracellular masses of cellulose called pellicles. The pellicles resemble a nonwoven fabric and can be grown in shapes as complicated as a glove (15). Also, the synthesis of cellulose by an individual bacterium, *Acetobacter xylinum*, can be observed directly with a microscope (16). Threads of bacterial cellulose grow to a length of a meter, compared to a few centimeters for cotton. Algal celluloses are of research interest because they occur in large and well-oriented crystallites. Superior structural data can be obtained by various experimental methods when crystallites are larger. However, ramie is also used for such experiments because it represents commercial celluloses better than do algal or bacterial cellulose. Ramie fibers contain smaller but highly oriented crystallites.

Only limited success has rewarded attempts to produce cellulose *in vitro*. Enzymes extracted from bacteria do not synthesize cellulose as efficiently as they do *in vivo*, even when the enzymes are activated (17). The catalytic subunit of a cellulose-synthesizing enzyme from *Acetobacter* has recently been cloned so details of the biosynthesis of cellulose in bacteria are emerging (18,19). Electron microscopy has revealed complexes that appear to be the *in vivo* sites of cellulose synthesis (20), although this is controversial and an alternative has been advanced (21,22). The complexes are linear in bacteria and some algae, but are rosette-shaped in other algae and in higher plants (23). The differences in synthesizing bodies, and the difference in the abilities of the enzymes to synthesize cellulose *in vitro*, suggest that several synthesizing mechanisms are used by biological systems. Cellulose may also be synthesized from β -cellobiosyl fluoride by reversing the action of an enzyme that usually degrades cellulose (24). Biosynthesis and biodegradation of cellulose have been reviewed (25).

Preparation

Most manufacturers of cellulosic products begin their work with cellulose that is in the form of pulp (qv). Pulping partially separates cellulose from the lignin (qv) and hemicelluloses (qv), leaving it in a fibrous form that is more susceptible to chemical treatment than the starting material. After pulping, the pulp is purified and otherwise treated to tailor it to the required specifications. Following drying, the pulp is shipped in large rolls.

Pulping. Mechanical and or chemical methods are used for pulping. Lignin softens at lower temperatures than cellulose, a difference that is the main basis for the separation. The exact structure of lignin is unknown and proposed mechanisms of delignification are somewhat speculative. Removal of

the lignin requires the opening of the porous cell wall system during pulping and pulp washing.

In mechanical pulping (stone grinding of wood billets) and in mechanical and thermochemical wood chip refining, most of the wood's substance is retained, including the lignin. Thus the yield is high and the amount of waste, which causes pollution, is relatively small. To liberate the cellulose fibers more fully without substantial mechanical defibration, chemical methods are used. In modern chemical pulping it is an economic necessity to recover the chemicals and to dispose of the organic waste liquor substances by combustion with adequate heat recovery. The related equipment costs are a large part of the total mill investment. In designing new mills, energy efficiency, chemical recovery, and measures to avoid water pollution are very important.

In chemical pulping, the wood is first reduced to chips, the size and uniformity of which are important for best penetration of the pulping liquors. Most pulping processes are designed to retain some of the hemicelluloses and lignin substances, as appropriate for specific final products. The properties of the final products such as the bulk, tear, burst, and tensile strengths, the folding endurance, and the optical properties such as brightness and opacity depend partly on the extent of removal of lignin and hemicelluloses during pulping.

Both the sulfite and alkaline (kraft) methods can be modified to produce high purity chemical cellulose. These pulps, usually in the form of "dissolving pulps," are not only mostly free of lignin and hemicellulose, but the molecular weight of the cellulose is degraded. This increases solubility in alkali and provides desired viscosity levels in solution. These dissolving pulps are used to make derivatives such as sodium cellulose xanthate [9051-13-2], via alkali cellulose, and various esters and ethers (see CELLULOSE ESTERS; CELLULOSE ETHERS).

Sulfite Processes. Various types of wood pulping are practiced in hot sulfite solutions with pH values ranging from 1.2 to 11. As a general rule, pulping at low pH causes more thorough removal of lignin and hemicellulose and also degrades the cellulose more. At pH values less than 2 there is considerable hydrolysis of hemicellulose and some of the cellulose, so this method is especially good for producing dissolving pulps.

Bisulfite pulping in the pH range of 2–6 is used on a variety of wood species. The resulting pulps are easily bleached. In these milder conditions the liquor is forced to circulate during cooking. Sodium-based bisulfite pulping gives higher brightness of unbleached pulp, resulting in higher quality. Two distinct two-stage processes using magnesium-based liquor are also in commercial use.

Calcium, magnesium, sodium, and ammonium hydroxides are used as bases to raise pH, partly to neutralize acids such as acetic acid that are split off from the hemicellulose in the wood during cooking. In the neutral sodium sulfite process (pH 7–9), the delignification is slow and hydrolysis of hemicellulose is reduced. The process is used mainly on hardwood, producing stiff pulps that are accordingly used in corrugated paperboard. Even higher pH levels (9–11 at cooking temperature) have been used, giving strengths similar to the alkaline processes and avoiding the kraft odor associated with those processes.

Alkaline (Kraft) Processes. Caustic soda pulping is the oldest alkaline process. It uses dilute sodium hydroxide solutions as the pulping agent and is in limited commercial use at present. Sulfate (kraft) pulping is the most significant process. It uses sodium sulfate (salt cake) as the source of the alkali. Kraft pulping liquor contains caustic soda and sodium sulfide. Sodium sulfide increases delignification and also pulp strength. In polysulfide pulping excess sulfur is present, resulting in some hemicellulose stabilization and yield increase.

Papers made from kraft pulps are strong, with especially high burst and tensile strength as well as folding endurance. However, their strength development in beating is slow compared with that of acid sulfite pulps. Unbleached kraft pulps have low brightness. Their strong coloration requires bleaching in up to six stages. The residual lignin is chemically changed and possibly grafted onto fibrous cellulose.

Two-stage prehydrolysis kraft cooking is used to produce dissolving pulps from hardwoods. Prehydrolysis consists of either liquid-phase cooking in acidified water or high pressure steam treatment. Acetic acid split from the wood aids in the hydrolysis of hemicellulose and also in the partial cellulose chain splitting necessary to reduce viscosity for chemical conversion into soluble cellulose derivatives. Subsequently, kraft cooking time is extended to promote lignin dissolution. The alkaline liquor also degrades the cellulose chains. Dissolving pulps used for the production of viscose and acetate must have uniform chain length distribution and be especially pure. Drawbacks of commercial kraft pulping include emissions of malodorous gases and a large capital investment.

The oxygen–alkali system is a fairly recent commercial development that avoids the use of sulfur compounds. Its mechanism of delignification has been investigated and the activation energy determined (26). Oxygen–alkali pulping produces good pulp brightness but low tear strength, indicating fiber damage.

Purification. Bleaching refers to all of the stages of pulp manufacturing between the completion of the pulping stage and the beginning of the stock preparation stage. The pulp producer takes several steps to provide the exact fibers specified by manufacturers of paper or chemical cellulose derivatives. Typically, purchase contracts request fibers characterized by well-defined physical, chemical, and optical attributes. A complete description of the overall process of pulp production is found in reference 27. A description of the technical details of bleaching is also available (28) (see BLEACHING, PULP AND PAPER).

The bleaching process removes the color bodies associated with the lignin and other impurities that survive the pulping operation. At the same time, it is possible to remove hemicellulose and resinous materials. In the ultimate purification process the steps are also designed to determine the chain length of the cellulose molecule (molecular weight) and the physical length of the fibers (fiber-length distribution). Such a procedure may require 11 or 12 steps to produce pulp for manufacture of cellulose films, sausage casings, textile fibers, and thickening agents. Chlorination, hypochlorite bleaching, chlorine dioxide bleaching, and extraction with concentrated NaOH are used, with intermediate alkaline extraction, ie, washing after each oxidative stage. On the other hand, most newsprint receives a single-step reductive brightening. The one-step processes for producing newsprint pulp and similar nonpermanent products are minimum bleaching procedures, designed to merely whiten the fibers to an acceptable level without causing weight loss or other physical effects.

Further Preparative Reactions. When pulps are to be used in the production of materials that do not retain the original fiber structure, such as rayon or cellulose acetate film, the lignin, hemicellulose, and other components must be reduced to the lowest possible concentrations. A surfactant (ionic or nonionic) is often added during a hot, weakly alkaline extraction step after chlorination. Another approach, sometimes used in addition to the surfactant step, is to treat the pulp with 6–10% NaOH after most of the oxidative bleaching is finished. This treatment removes most of the hemicellulose. In most purification plants the final stage includes use of sulfuric acid; chelators are optional.

Steam Explosion. Steam explosion (29–35) is another way to break down lignocellulose [11132-73-3] into a fibrous powder that has substantially increased accessibility to chemical or biological agents. Moisture-saturated wood chips, straw, or other materials are subjected to high pressure (3.5–4.0 MPa and temperature (200–250°C), followed by rapid decompression. The temperatures and pressures used depend on both the type of starting material and the desired use of the product, with more severe conditions providing greater separation of the components and greater degradation of the cellulose molecular weight. Several of the most intense technologies yield nearly complete separations into cellulose, lignin, and xylan; products such as cellulose acetate [9004-35-7], vanillin [121-33-5], and xylose [58-86-6] that require high quality starting materials can even be made from waste materials. Milder conditions are used as an alternative to conventional pulping for the manufacture of high yield pulps for the manufacturing of paper. Lignocellulose given weaker treatments can be formed into molded building materials. Steam exploded wood can be fed to ruminants because of its enhanced digestibility. It is also a suitable substrate for fermentation into alcohol, etc.

Microcrystalline Cellulose

Pulverized forms of woodpulp have been widely used as fillers in some foods and pharmaceuticals. However, their utility is limited because the highly fibrous form results in poor mouthfeel. This problem can be overcome by reducing the woodpulp fibers to colloidal microcrystalline cellulose (36). It is made by hydrolysis with hydrochloric acid to the point of leveling off degree of polymerization. In aqueous suspensoids, these much finer particles have a smooth texture resembling uncolored butter and pseudoplastic properties including stable viscosity over a wide temperature range. It can therefore be used as a low calorie substitute for fat (see FAT SUBSTITUTES). Microcrystalline celluloses are important for their heat stability, ability to thicken with favorable mouthfeel, and flow control. They extend starches, form sugar gels, stabilize foams, and control formation of ice crystals. A few of the foods in which microcrystalline cellulose has been commercially successful are fillings, meringue (cold process), chocolate cake sauce (frozen), cookie fillings, whipped toppings, and imitation ice cream for use as a bakery filling. In the pharmaceutical industry, microcrystalline cellulose is used mostly for tableting. It is used as an excipient to assist in the flow, lubrication, and bonding properties of the ingredients to be tableted, to improve the stability of the drugs in tablet

form, and especially to provide for rapid disintegration in the stomach.

Over 250,000 metric tons of microcrystalline cellulose have been sold since its commercialization in 1962 and demand continues to increase. Its utility has led to development of other colloidal polymer microcrystals (see COLLOIDS). For example, polyamides and polyesters from recycled materials can be biodegraded to give microcrystals having a size of 30 nm (37).

Structure and its Relation to Chemical and Physical Properties

The chemical and physical properties of cellulose depend in large measure on the spatial arrangements of the molecules. Therefore, cellulose structures have been studied intensively, and the resulting information has been important in helping to understand many other polymers. Despite the extent of work, however, there are still many controversies on the most important details. The source of the cellulose and its history of treatment both affect the structure at several levels. Much of the industrial processing to which cellulose is subjected is intended to alter the structure at various levels in order to obtain desired properties.

Modeling studies usually show that the lowest energy for an isolated cellulose molecule occurs when it is completely extended (Fig. 1) (38). When dissolved, cellulose molecules are still fairly extended, but exist as random coils with relatively large distances between their ends (Fig. 2) (39). The individual molecules often coalesce to form straight microcrystals (microfibrils) that are 3–30 nm across and perhaps 7 μm in length (Fig. 3) (40,41). These microcrystals can be bent (42,43). In some cases, such as cotton, the microfibrils organize into macrofibrils 60–300 nm wide. The microfibrils or macrofibrils are then organized into fibers. Diffraction contrast electron microscopy of algal cellulose shows that cross-sections perpendicular to the long axes of microfibrils are nearly square (40,41). This technique produces images that show extended cellulose molecules running parallel to the long axis of the microfibril (40).

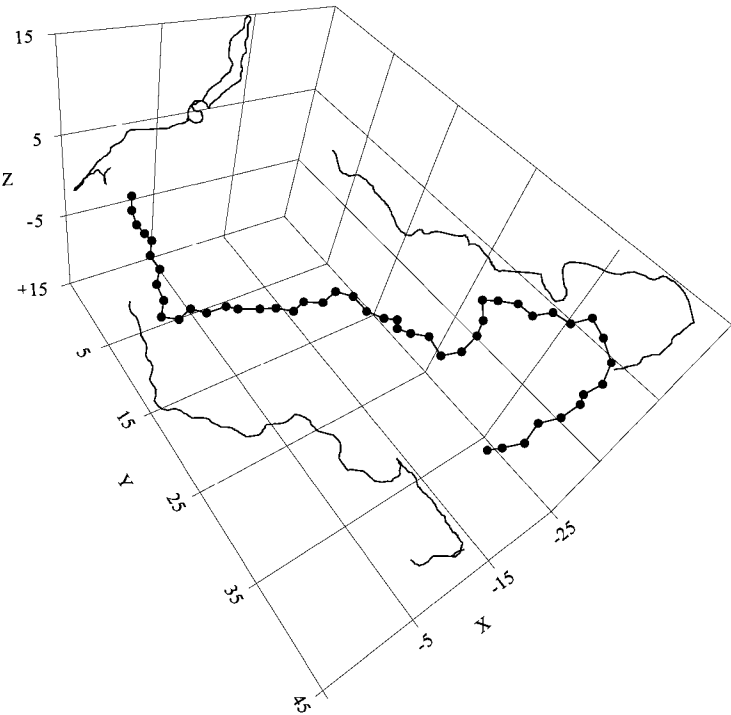


Fig. 2. A representation of the cellulose chain in solution, projected against three two-dimensional surfaces. The circles represent the oxygen atoms that link the individual glucose residues, and the lines take the place of the sugar residues. This result of a modeling study (39) indicated a molecule somewhat more flexible than found experimentally.

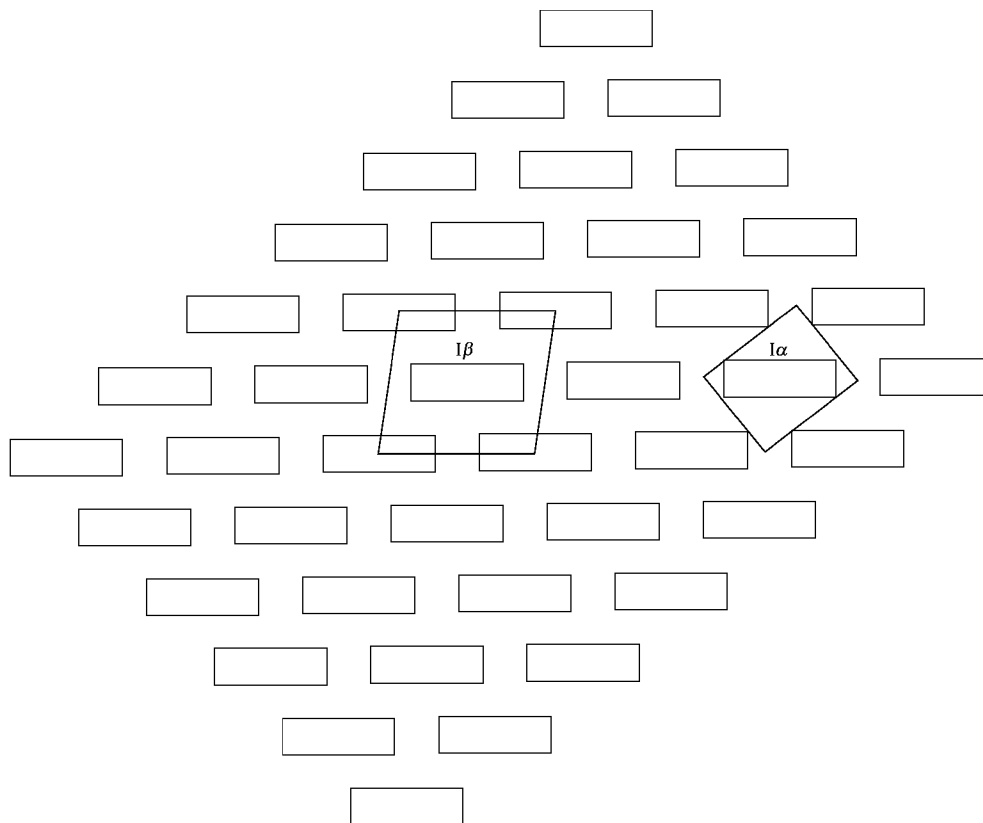


Fig. 3. A cross-section of a nearly square cellulose microfibril, with the individual molecular chains shown as rectangles. Also shown are the one- and two-chain unit cells of $I\alpha$ and $I\beta$. This view of the microfibril is parallel to the long axis. The chains are arranged so that the edges of the crystal correspond to diagonals of the two-chain unit cell, or the sides of the one-chain cell (40,41).

Cotton fibers have a complex, reversing, helical arrangement of macrofibrils. The properties of cotton fabrics are therefore distinct from properties of fabrics made of the simpler ramie and linen fibers. Among cotton varieties, variations in this architecture are associated with differences in strength and other qualities. Most cellulosic materials have pores into which reagents must penetrate in order to react, and variations in these pore sizes govern the extent of reaction and quality of finished products (44). An important change in the pore structure occurs when the moist, previously unopened cotton boll opens and dries out. The changes of pore structures during drying occur because cellulose–water hydrogen bonds change to cellulose–cellulose hydrogen bonds.

The degree of crystallinity of cellulose also affects properties. Cotton, perhaps the most crystalline of the commercial celluloses, has about 20% disordered material, including chain ends and crystallite surfaces. About half of the molecules in cotton are on surfaces of microfibrils, although these surfaces may have limited accessibility because of the macrofibrillar structure. Variations in molecular shape might sometimes occur in amorphous regions, such as twisting of the chain backbone from its usual ribbon shape, or even, although rarely, changing the chair form of the glucopyranose rings to some other shape. Cellulose can be decrystallized mechanically by ball-milling or chemically (45,46). Chemical and biochemical reactions of less crystalline cellulose are usually more rapid than those of the crystalline materials.

Cellulose crystallizes in several different forms (allomorphs or polymorphs), depending on source and treatment. In some cases, more than one form is present in a sample, owing to incomplete conversion. In such instances, the fraction of each allomorph, quickly determined with x-ray diffraction, indicates the effectiveness of the conversion treatment. During the allomorphic conversions, many other changes are likely to occur at several levels of structure. Therefore, it is risky to interpret changes in properties solely in terms of crystal form and the underlying changes in chain packing, hydrogen bonding, or molecular conformation. That disclaimer aside, the particular crystal form is an important aspect of solid cellulose.

In all well-characterized allomorphs the chains are thought to have similar extended shapes that differ in minor details, such as the orientations of the rotatable hydroxyl and primary alcohol groups. Changes in these groups permit a variety of hydrogen-bonding and crystal-packing arrangements and result in different availabilities and accessibilities of hydroxyl groups to reagents. Extended chains pack efficiently only if their long axes are parallel. There are three such ways in which chains could pack in the monoclinic or triclinic crystals found for cellulose (47). If the chains alternate in direction, with half the reducing ends at each end of the microfibril, the packing is "antiparallel." If all reducing ends are at one of the ends of the microcrystal, the chain packing is "parallel up." If they are all at the other end, the packing is "parallel down." The subtle distinction between the up and down types of packing escaped early workers in the field.

Crystal Structure Studies. Cellulose fibers can be studied by diffraction of x-ray, electron, or neutron beams. However, the small quantity of data from fiber diffraction (30–50 spots) is insufficient for complete structural determination. Consequently, structural studies by diffraction are augmented by molecular models, and are therefore less rigorous than typical, single-crystal diffraction studies of small molecules. Other techniques, such as solid-state nuclear magnetic resonance and infrared spectroscopy, have furnished qualitative information regarding chain symmetry and hydrogen bonding. Investigations by electron microscopy rely increasingly on techniques such as diffraction contrast.

In a study of fiber crystal structures by diffraction, the dimensions of the unit cell are determined first. The unit cell is the smallest spatial unit (along with its atomic contents) that, through translational symmetry, can generate the entire crystal. The dimensions are indicated by the positions of the spots on the diffraction diagram. Next, the intensities of the spots on the diffraction pattern are measured. Model cellulose chains are placed at trial positions in the unit cell and the intensities are calculated. The model that gives the best agreement, ie, lowest R value, between the observed and calculated intensities corresponds to the final structure. Often the energies of the trial structures are calculated as well, and selection of the final structure takes into account both the extent of disagreement with the diffraction data and the energetic stability of the model (48). Errors in the measured intensities may be important (49), but a more definitive approach is not available.

Unit cells of pure cellulose fall into five different classes, I–IV and x. This organization, with recent subclasses, is used here, but Cellulose x is not discussed because there has been no recent work on it. Crystalline complexes with alkali (50), water (51), or amines (ethylenediamine, diaminopropane, and hydrazine) (52), and crystalline cellulose derivatives also exist. Those structures provide models for the interactions of various agents with cellulose, as well as additional information on the cellulose backbone itself. Usually, as shown in Figure 1a, there are two residues in the repeated distance. However, in one of the alkali complexes (53), the backbone takes a three-fold helical shape. Nitrocellulose [9004-70-0] helices have 2.5 residues per turn, with the repeat observed after two turns (54).

Cellulose I. The majority of celluloses in the native state were previously thought to have the same crystal structure (Cellulose I), varying only in perfection of the crystallites. Now, at least two different crystal structures are known for these materials, named $I\alpha$ and $I\beta$. These two phases coexist in

many natural cellulosic materials. In addition, a few algae and bacteria make only Cellulose II, and some immature or primary wall cellulose has the Cellulose IV form.

Clues to the two-phase composition of most Cellulose I s were not correctly interpreted until recently. For example, infrared spectra for algal and bacterial celluloses are known to differ from those of cotton and ramie (55). Also, eight-chain unit cells were proposed for algal and bacterial Cellulose I (56) rather than the two-chain Meyer and Misch unit cell for ramie (57). Those troubling details were amplified by the discovery of differing amounts of the I α and I β forms in a number of materials, principally through solid-state nmr studies (58). Treatment at 260°C in dilute NaOH converts algal cellulose, composed of nearly equal amounts of I α and I β , to pure I β material (59). The use of electron diffraction on small areas of large microfibrils from the alga *Microdictyon tenuis*, shows that the I α and I β forms both occur in the same microfibril (60). One set of diffraction spots from these microfibrils corresponds to a one-chain triclinic unit cell that yields the I α components of the nmr spectrum. The other diffraction pattern is from the I β unit cell, which is similar to the monoclinic, two-chain Meyer and Misch cell. At some places along the microfibril the resulting diffraction pattern is a mixture of the two sets of intensities.

The superimposition of diffraction spots from both phases gives the previously reported pattern that was thought to require an eight-chain unit cell. In the I α structure, because of its one-chain unit cell, all chains must have parallel packing. Since the I α and I β structures exist in the same microfibril of cellulose, the chains in the I β structure should also be parallel.

The detailed molecular structures of I α and I β have not been determined. In previous work that incorrectly treated mixtures of I α and I β as a single phase, the chains were found to be arranged in sheets, comprising the horizontal rows in Figure 3. In most of the recent proposals for Cellulose I, hydrogen bonds connect the chains within the sheets, but do not extend between the sheets. As shown in Figure 3, the overall packing for I α and I β could be quite similar. In both forms, a second sheet is displaced along the chain axis (perpendicular to the plane of Figure 3) relative to the first by about 0.25 nm. The difference between the two types of packing is that the third sheet is shifted again by about 0.25 nm in I α , while the third sheet in I β is shifted roughly 0.25 nm, placing it at the same height as the first sheet. These distances are relative to a base plane parallel to the plane of the drawing in Figure 3.

It was proposed that the celluloses of commerce such as wood, cotton, and ramie have mostly I β structure (61). A more recent study using infrared and electron diffraction supports the similarity of the I β celluloses from different sources (62). There is at least one question regarding whether the dominant phase in commercial celluloses is the same as the I β phase in algal and tunicate cellulose (apparently a pure I β material). Heating ramie or cotton to 260°C in glycerol converts it to Cellulose IV, whereas heating the I α -I β mixtures of algal celluloses to the same temperature in dilute alkali yields especially pure I β . A study of ramie cellulose proposed that both up and down chains exist, statistically, at the same crystal sites (63). However, the R factor is not greatly better than for more conventional packing arrangements, considering the additional freedom in the model.

The dimensions of the unit cells deduced for Cellulose I seem to depend on the kind of plant that is the source of the cellulose; wide ranges are reported (64). Since most Cellulose I s are mixtures of two or more structures, with mostly overlapping diffraction spots, the various observed dimensions could result from different amounts of the I α , I β , and possibly other forms.

Cellulose II. Cellulose II results from the crystallization of dissolved cellulose, with the best results obtained at temperatures near 0°C. Another way to make Cellulose II is by repeated mercerization, the swelling of cellulose in strong alkali, eg, 23% NaOH, followed by rinsing and drying. Typical one-step commercial mercerizing of cotton yarn causes only partial conversion. The swelling and deswelling is accompanied by the formation of several successive soda-cellulose complexes. If allowed to relax, the fibers shrink in length. If they are not allowed to shrink during soaking in alkali, extensive conversion does not occur. Cellotetraose and higher cellooligosaccharides give diffraction patterns similar to that of Cellulose II. Yet another way to induce Cellulose II is to repeatedly wet and dry decrystallized cellulose. Reversion of Cellulose II to Cellulose I is unknown, so Cellulose II is probably more stable than I. Figure 4 compares the dimensions of II with the other unit cells.

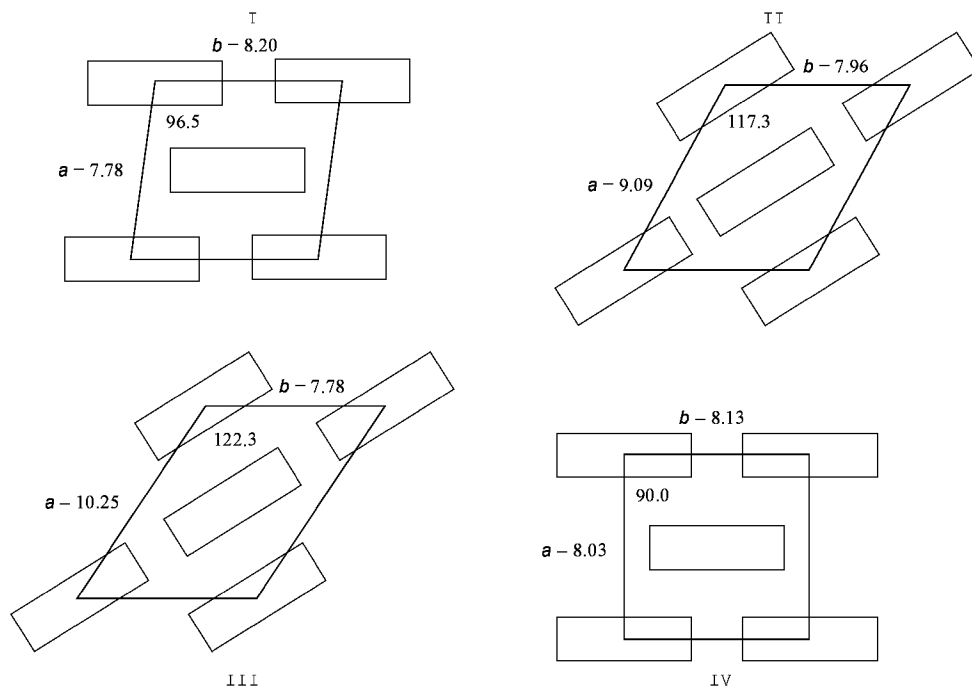


Fig. 4. Comparisons of the unit cells proposed for Cellulose I-IV. In all cells, the c dimension (perpendicular to the plane of the drawing) is ca 1.034 nm. The dimensions (in nm) were taken from Refs. 65-68.

Mercerized cellulose fibers have improved luster and do not shrink further. One of the main reasons for mercerizing textiles is to improve their receptivity to dyes. This improvement may result more from the disruption of the crystalline regions rather than the partial conversion to a new crystal structure. A good example of the fundamental importance of the particular crystal form is the difference in rate of digestion by bacteria. Bacteria from cattle rumen rapidly digest Cellulose I but degrade Cellulose II very slowly (69). Thus allomorphic form can be an important factor in biochemical reactions of cellulose as well as in some conventional chemical reactions.

Rayon, made from dissolved and regenerated wood and/or cotton, has the Cellulose II structure. Besides garments, rayon is used for tire cord and industrial belting. Typical rayon yarns have lower tensile strength than Cellulose I yarns, but Fortisan, a heterogeneously saponified cellulose acetate formerly made by Hoechst-Celanese, is a high strength rayon yarn, mostly because its crystallites are highly aligned along the fiber axis. The variables in the process of producing rayon fibers allow a large variety of performance characteristics see (FIBERS, REGENERATED CELLULOSES).

Similar models for the crystal structure of Fortisan Cellulose II came from two separate studies despite quite different measured values of the diffraction intensities (66,70). Both studies concluded that the two chains in the unit cell were packed antiparallel. Hydrogen bonding between chains at the corners and the centers of the unit cells, not found in Cellulose I, was proposed to account for the increased stability of Cellulose II. The same model, with

varied orientations of the hydroxyl groups on the crystallite surfaces, was proposed for mercerized Cellulose II (71).

Accepting a parallel structure for Cellulose I and an antiparallel structure for II makes the conversion difficult to explain because cellulose retains its fibrous form during mercerization. Two proposed mechanisms (50,71) depend on the presence of an adjacent microfibril oriented in the opposite direction, as found for algal and bacterial cellulose. In these proposals, the sheets of chains or individual chains of the two swollen microfibrils merge or "interdigitate," forming a microcrystal with antiparallel chains. In another study, parallel chain structures for Cellulose II fit the diffraction data and energy criteria as well as antiparallel models did (72). Those results contrast sharply with other findings (73,74). Ultimately, the correct structures must explain the irreversibility of the I → II conversion and the shrinkage during mercerization given scant attention so far.

Cellulose III. Cellulose III results from treatment of cellulose with liquid ammonia (ammonia mercerization) or amines. Cellulose III can be made from either Cellulose I or II. When treated with water, Cellulose III can revert to its parent structure. Some cellulose III preparations are much more stable than other preparations. The intensities on diffraction patterns from Cellulose III differ slightly depending on whether the Cellulose III was made from Cellulose I or II, and thus these allomorphs are called III_I or III_{II}. Workers studying III concluded, based partly on the results of I and II, that the packings of III_I and III_{II} are parallel and antiparallel, respectively (67). III_{II} also is thought to have hydrogen bonds between the corner and center chains.

Treatment of the algal cellulose (mixture of Iα–Iβ) from *Valonia* in ethylenediamine to give Cellulose III_I simultaneously induced subfibrillation in the initial microfibril (75). Thus crystallites 20 nm wide were split into subunits only 3–5 nm wide, even though the length was retained. Conversion of this III_I back to I gave a material with an electron diffraction pattern and nmr spectrum similar to that of cotton Cellulose Iβ.

Cellulose IV. Like Cellulose III, Cellulose IV preparations can revert to their parent Cellulose I or II structures. These forms can be prepared by treating Cellulose I, II, or III in glycerol at temperatures ca 260°C. Long-chain oligomers, eg, 20 residues, crystallize from solution at high temperatures (90°C) as the IV_{II} form (76). Immature native celluloses give diffraction patterns that indicate the structure to be poorly crystalline Cellulose IV_I (77). IV_{II} is thought to have hydrogen bonds between the corner and center chains (68).

Other Structural Studies. Other differences among cellulosic materials at the microfibril level are not explained by any of the above considerations. For example, groups of hydroxyl hydrogen atoms subject to substitution on cellulose surfaces differ greatly among the celluloses from various sources, regardless of the underlying crystal structure. Thus substitution reactions of *Valonia* Cellulose I give a mixture of derivatives similar to those of mercerized cotton (Cellulose II) (78). This is puzzling because electron microscopy shows that at least some celluloses have well-defined crystallite surfaces with precise underlying chain orientations (43) (Fig. 3).

Two categories of methods, in addition to diffraction, indicate the degree of crystallinity (79). Those involving chemical reaction include acid hydrolysis, formylation, periodate oxidation, and chemical microstructural analysis (cma). Cma requires reaction with *N,N*-diethylaminoethyl chloride [100-35-6] and is based on the availability of the hydroxyl group on carbon 3. Other methods involving sorption include deuteration, moisture regain, and iodine sorption. Both chemical reaction and sorption techniques differ from physical measurements because they measure the fraction of the cellulose that is not readily accessible to a specific reagent. The determined fraction of ordered cellulose varies depending on the method.

The accessibilities of cotton fibers (44) have been assessed by solute exclusion. Both static and column chromatographic techniques (79) have been used. Series of water-soluble molecules of increasing size are used as molecular probes or "feeler gauges." These include sugars of low molecular weight, ethylene glycols, glymes, and dextrans. Each molecule used as a probe should penetrate the cellulose being investigated and not be adsorbed on the cellulosic surfaces. The static measurement is based on addition of water-swollen cellulose to a solution of the molecular probe. Water in pores accessible to the solute dilutes the solution. In the chromatographic technique, glass columns are packed with cellulose and the elution volumes of the series of molecular probes are used to deduce structural differences. Similar information is obtained from both methods. Results give the internal volume available to the probes.

Chemical Reactivity

Cellulose is chemically like other carbohydrates (qv) that consist of pyranose rings bearing hydroxyl groups. These glucose residues include a reducing end unit, a nonreducing end unit, and intermediate units. Most celluloses have a high degree of polymerization; the intermediate glucose residues determine the chemical and physical properties and the end units may be ignored. The glycosidic bonds in cellulose are strong and this polymer is stable under a wide variety of reaction conditions. It is a generally insoluble, highly crystalline polymer.

Cellulose can be degraded by either acid or alkali. The glycosidic bond is susceptible to acid catalyzed hydrolysis. High yields of glucose can result when hydrolysis proceeds for a long enough time, needing days or weeks. After a few hours under conditions such as room temperature and HCl concentrations around 10 N or 0.25 M H₂SO₄ at 100°C, noncrystalline cellulose is lost, leaving a more crystalline material. A leveling off degree of polymerization (LODP) of 150 or 180 glucose residues is reached (80), with the length depending on the source of the cellulose. Explanations based on chain-folding (81) for the various LODP values from different celluloses are not consistent with evidence from other studies of cellulose structure. However, except for a proposal of periodic weak zones (disruptions in the structure of the microfibril), no explanation has been put forth.

Cellulose is also degraded by alkali (82) but in an entirely different manner. Where oxygen has been excluded, cellulose undergoes endwise degradation, scission of the glycosidic linkages, and, under certain conditions, breakdown to low molecular weight organic acids.

Oxidation under moderate conditions (83) yields solid products referred to as oxycelluloses. This general term describes various products that must be qualified by indicating the oxidant employed. Among oxidants used are periodate, dinitrogen tetroxide, and sodium hypochlorite. Cellulose is particularly susceptible to oxidation under alkaline conditions.

Industrially important chemical modifications of this polymer generally involve reaction with its 2, 3, and 6 hydroxyl groups. These reactive sites undergo most of the reactions characteristic of alcohols. Etherification and esterification are of particular importance for cellulose. Cross-linking of the polymer chains gives durable press properties to cellulosic textiles and dimensional stability to wood products. These reactions with the hydroxyl groups usually take place under heterogeneous conditions because of the insoluble and crystalline nature of cellulose. Under such mild heterogenous conditions, the reactivities of hydroxyl groups may depend on whether they are involved in hydrogen bonds. Compared with soluble polysaccharides, therefore, the extents of such reactions are inhibited.

Cellulose Solvents

Cellulose is soluble only in unusual and complex solvent systems. The subject has been reviewed (84–87). Commercially, dissolving pulps, which have lower molecular weights, are used along with strong alkali and derivatization. Cellulose subjected to high temperature and pressure during the steam explosion process can be dissolved in strong base (88).

Solvents for cellulose are central to the rayon and cellophane industries. The solvents fall into several categories: solvents discussed here do not include processes where cellulose is converted to a derivative that is subsequently dissolved in another medium. For example, cellulose acetate is soluble in acetone, but this is not a solution of cellulose. However, the viscose process that forms a cellulose xanthate [9032-37-5] derivative, from which cellulose is readily regenerated, is generally considered to use a cellulose solution because solvation and derivatization occur simultaneously. The viscose process is the most important industrial method for making cellulose solutions (89). Alkali cellulose [9081-58-7], pulp swollen in NaOH, is pressed and aged to reduce molecular weight. Xanthation, a reaction with CS₂, takes place in a vessel that contains an inert atmosphere because CS₂–air mixtures are explosive. The orange xanthate is subsequently dissolved in aqueous alkali to make the spinning dope. The dope is pumped through spinnerets in which there are from 14 to 40,000 holes. The spun dope is converted back to cellulose by the sulfuric acid in the coagulating bath. Another system with simultaneous derivatization and dissolution uses dimethyl sulfoxide and formaldehyde (90).

Several solvents, such as cupriethylenediamine (cuen) hydroxide [111274-71-6], depend on the formation of metal–ion complexes with cellulose. Although not as widespread in use as the viscose process, cuen and its relatives with different metals and ammonium hydroxide find substantial industrial use (87). The cadmium complex Cadoxen is the solvent of choice in laboratory work (91).

Aqueous salt solutions such as saturated zinc chloride [7646-85-7] or calcium thiocyanate [2092-16-2] can dissolve limited amounts of cellulose (87). Two non-aqueous salt solutions are ammonium thiocyanate [1762-95-4]–ammonia and lithium chloride [7447-41-8]–dimethylacetamide [127-19-5]. Solutions up to about 15° º can be made with these solvents. Trifluoroacetic acid [76-05-1]–methylene chloride [75-09-2] and N-methylmorpholine N-oxide [7529-22-8]–H₂O (92–94) are two other solvent systems that have been studied (95).

The primary driving forces behind investigation of new solvents include environmental concerns and the ability to form liquid crystals in the new solvent systems. By analogy with Kevlar, a synthetic aromatic polyamide fiber, spinning from a liquid crystalline solution should yield cellulose fibers with improved strength, as has been demonstrated in laboratory experiments.

Liquid Crystals

Many cellulose derivatives form liquid crystalline phases, both in solution (lyotropic mesophases) and in the melt (thermotropic mesophases). The first report (96) showed that aqueous solutions of 30° º hydroxypropylcellulose [9004-64-2] (HPC) form lyotropic mesophases that display iridescent colors characteristic of the chiral nematic (cholesteric) state. The field has grown rapidly and has been reviewed from different perspectives (97–101).

The separation of liquid crystals as the concentration of cellulose increases above a critical value (30° º) is mostly because of the higher combinatorial entropy of mixing of the conformationally extended cellulosic chains in the ordered phase. The critical concentration depends on solvent and temperature, and has been estimated from the polymer chain conformation using lattice and virial theories of nematic ordering (102–107). The side-chain substituents govern solubility, and if sufficiently bulky and flexible can yield a thermotropic mesophase in an accessible temperature range. Acetoxypropylcellulose [96420-43-8], prepared by acetylating HPC, was the first reported thermotropic cellulosic (108), and numerous other heavily substituted esters and ethers of hydroxyalkyl celluloses also form equilibrium chiral nematic phases, even at ambient temperatures.

Substituted cellulose chains have chiral twists. This leads to chiral nematic liquid crystals, in which the polymer is oriented in macroscopic helicoidal structures. If the pitch of these helicoidal structures is of the same magnitude as the wavelength of visible light, the samples show striking optical properties, in particular the reflection of circularly polarized light with a wavelength related to the pitch. The wavelength of the reflected light depends on factors such as the nature of the side-groups, the degree of substitution, the molecular weight of the polymer, temperature, the nature of the solvent, and the polymer concentration. Hydroxypropylcellulose and several of its ether and ester derivatives form right-handed nematic phases (96,108–110). Ethylcellulose [9004-57-3] in glacial acetic acid gives a left-handed nematic phase (111). A change in the nematic chirality may occur with a change in the side-group substituents (112–115) and solvent (116,117). Thermally induced inversions of the twist sense have been reported for oligomers of tri-O-2-(2-methoxyethoxy)ethylcellulose [123423-08-5] (TMEC) and tri-O-heptylcellulose [100214-73-1] (118).

The helicoidal structure of such liquid crystals can be carried to the solid state by cross-linking (119,120) or by careful evaporation of solvent (121,122). Underivatized cellulose can also form ordered mesophases (123,124), and gel films precipitated from lithium chloride–dimethylacetamide retain some mesophase structure (122).

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CELLULOSE ACETATE AND TRIACETATE FIBERS.

See FIBERS, CELLULOSE ESTERS.

CELLULOSE DERIVATIVES.

See CELLULOSE ESTERS; CELLULOSE ETHERS.

CELLULOSE ESTERS

Organic esters,
Inorganic esters,

^b Unit molecular weight of acetyl group, CH₃CO, is 43.
^c Degree of acetylation is often expressed as percent combined acetic acid.

During World War I, cellulose acetate replaced the highly flammable cellulose nitrate coating on airplane wings and the fuselage fabrics. After World War I, it found extensive use in photographic and x-ray films, spun fibers, and molding plastics. Although cellulose acetate remains the most widely used organic ester of cellulose, its usefulness is restricted by its moisture sensitivity, limited compatibility with other synthetic resins, and relatively high processing temperature. Cellulose esters of higher aliphatic acids, C₃ and C₄, circumvent these shortcomings with varying degrees of success. They can be prepared relatively easily with procedures similar to those used for cellulose acetate. Mixed cellulose esters containing acetate and either the propionate or butyrate moieties are produced commercially in large quantities by Eastman Chemical Co. in the United States (Table 2). Bayer AG discontinued the production of mixed esters at Leverkusen in Germany in mid-1987 citing poor economics as the reason for the closing.

Table 2. Domestic and Foreign Producers of Cellulose Acetate

Producer	Country	Annual capacity, 10 ³ t
North America ^a		
Eastman Kodak Co. ^b	United States	197
Hoechst Celanese Corp.	United States, Canada, Mexico	241
Western Europe ^c		
Agfa-Gevaert	Belgium	5
Tubize Plastics ^d	Belgium	7
Rhône-Poulenc Chemie	France	25
Rhodia AG	Germany	>25
Industrias del Acetato de Celulosa	Spain	2
Courtaulds Fibres Ltd.	United Kingdom	54
Nelsons Acetate Ltd. ^e	United Kingdom	14
Asia		
Daicel Chemical Industries, Ltd.	Japan	100
Teijin Acetate Ltd.	Japan	11.8

^a CEH estimates as of Nov. 1, 1988 (4).
^b Also produces cellulose acetate butyrate (CAB) and cellulose acetate propionate (CAP) mixed esters.
^c CEH estimates as of Jan. 1, 1989 (4); Bayer AG (Germany) discontinued CAB CAP production at Leverkusen in mid-1987; capacity for resin-grade cellulose acetate flake had been reduced from 25,000 t in 1981 to 15,000 t prior to closing.
^d In 1984, PMC Inc. (United States) purchased Tubize Plastics SA from government owned Fabelta Tubize SA. This facility was sold to Rhône-Poulenc in Oct. 1988.
^e In 1988, Courtaulds took over Hercules' 50% interest in Nelsons Acetate.

Cellulose esters of aromatic acids, aliphatic acids containing more than four carbon atoms and aliphatic diacids are difficult and expensive to prepare because of the poor reactivity of the corresponding anhydrides with cellulose; little commercial interest has been shown in these esters. Of notable exception, however, is the recent interest in the mixed esters of cellulose succinates, prepared by the sodium acetate catalyzed reaction of cellulose with succinic anhydride. The additional expense incurred in manufacturing succinate esters is compensated by the improved film properties observed in waterborne coatings (5). Mixed cellulose esters containing the dicarboxylate moiety, eg, cellulose acetate phthalate, have commercially useful properties such as alkaline solubility and excellent film-forming characteristics. These esters can be prepared by the reaction of hydrolyzed cellulose acetate with a dicarboxylic anhydride in a pyridine or, preferably, an acetic acid solvent with sodium acetate catalyst. Cellulose acetate phthalate [9004-38-0] for pharmaceutical and photographic uses is produced commercially via the acetic acid–sodium acetate method.

Properties

The properties of cellulose esters are affected by the number of acyl groups per anhydroglucose unit, acyl chain length, and the degree of polymerization (DP) (molecular weight). The properties of some typical cellulose triesters are given in Table 3. In this series, with increasing acyl chain length from C₂ to C₈, the melting point, tensile strength, mechanical strength, and density generally decrease, whereas solubilities in nonpolar solvents and resistance to moisture increase. Fewer acyl groups per anhydroglucose unit, ie, increased hydroxyl content, increase the solubility in polar solvents and decrease moisture resistance. The physical and chemical properties of mixed esters vary according to the ratio of the esters used, eg, acetyl to butyl or acetyl to propionyl. General trends of the properties of mixed esters, such as cellulose acetate butyrate [9004-36-8] (CAB), as a function of composition are illustrated in Figure 3, in which increasing butyryl (decreasing acetyl) content increases flexibility, moisture resistance, and nonpolar solubility and decreases melting point and density.

Table 3. Properties of Cellulose Triesters^a

Cellulose ester	Shrinking point, °C	Mp ^b , °C	Water tolerance value ^c	Moisture regain ^d , %			Density, g/mL	Tensile strength, MPa ^e
				50%	75%	95%		
cellulose ^f				10.8	15.5	30.5	1.52	
acetate		306	54.4	2.0	3.8	7.8	1.28	71.6
propionate	229	234	26.9	0.5	1.5	2.4	1.23	48.0
butyrate	178	183	16.1	0.2	0.7	1.0	1.17	30.4
valerate	119	112	10.2	0.2	0.3	0.6	1.13	18.6
caproate	84	94	5.88	0.1	0.2	0.4	1.10	13.7
heptylate ^g	82	88	3.39	0.1	0.2	0.4	1.07	10.8
caprate	82	86	1.14	0.1	0.1	0.2	1.05	8.8

caprate ^h	87	88	0.1	0.2	0.5	1.02	6.9
laurate	89	91	0.1	0.1	0.3	1.00	5.9
myristate	87	106	0.1	0.1	0.2	0.99	5.9
palmitate	90	106	0.1	0.1	0.2	0.99	4.9

- ^a Ref. 6. Courtesy of the American Chemical Society.
- ^b Char point is 315°C or higher unless otherwise noted.
- ^c Milliliters of water required to start precipitation of the ester from 125 mL of an acetone solution of 0.1% concentration.
- ^d At 25% rh moisture regain for cellulose is 5.4%; for the acetate, 0.6%; for the propionate and butyrate, 0.1%; all others are zero.
- ^e To convert MPa to psi, multiply by 145.
- ^f Starting cellulose, prepared by deacetylation of commercial, medium viscosity cellulose acetate (40.4% acetyl content).
- ^g Char point 290°C.
- ^h Char point 301°C.

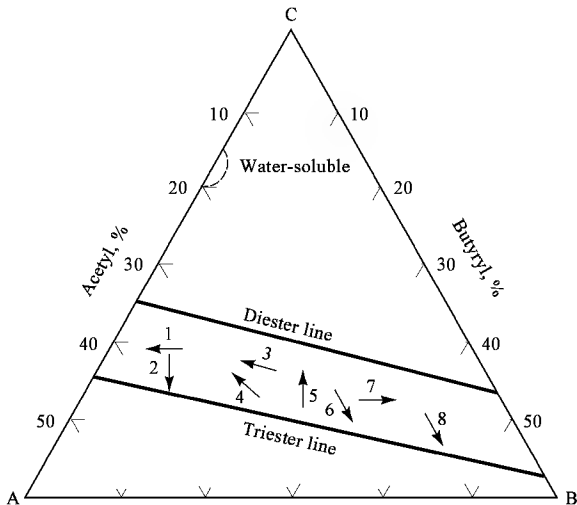


Fig. 3. Effects of composition on physical properties. A, acetyl; B, butyryl; C, cellulose. 1, increased tensile strength, stiffness; 2, decreased moisture sorption; 3, increased melting point; 4, increased plasticizer compatibility; 5, increased solubilities in polar solvents; 6, increased solubilities in nonpolar solvents; 7, increased flexibility; 8, decreased density (7).

The common commercial products are the primary (triacetate) and the secondary (acetone-soluble, ca 39.5% acetyl, 2.45 DS) acetates; they are odorless, tasteless, and nontoxic. Their properties depend on the combined acetic acid content (acetyl, see Table 1 and Figure 4) and molecular weight. Solubility characteristics of cellulose acetates with various acetyl contents are given in Table 4.

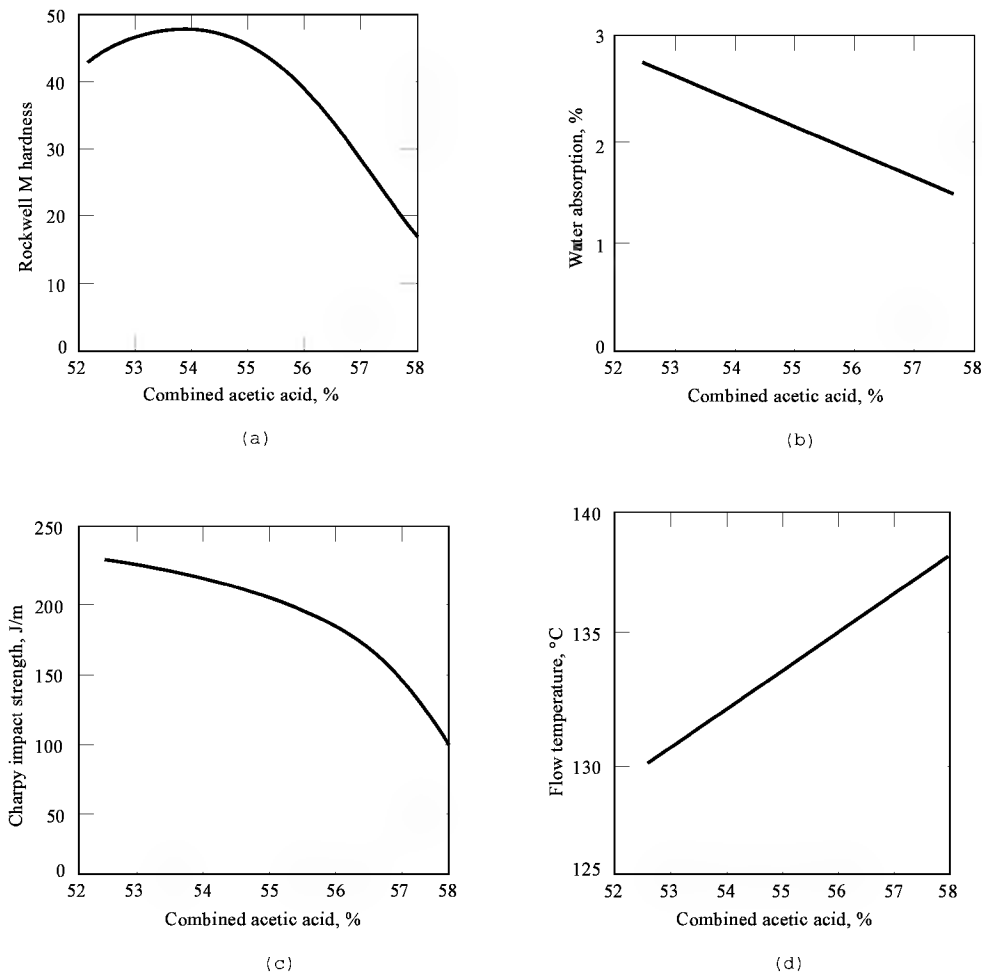


Fig. 4. Effect of combined acetic acid content on (a) hardness, (b) absorption, (c) impact strength, and (d) temperature of cellulose acetate (8). To convert J m to ft-lbs in., divide by 53.38.

Table 4. Solubility Characteristics of Cellulose Acetates

Acetyl, %	Soluble in	Insoluble in
43.0–44.8	dichloromethane	acetone
37–42	acetone	dichloromethane
24–32	2-methoxymethanol	acetone
15–20	water	2-methoxymethanol
<13	none of the above	all of the above

Cellulose triacetate [9012-09-3] has the highest melting point (ca 300°C) of the triesters; melting points generally decrease to a minimum of ca 230°C as the acetyl content decreases to 38–39% (secondary acetate).

Moisture sensitivity and vapor-permeability rate of cellulose acetate increase with decreasing acetyl (increasing hydroxyl) content. Thermoplastic characteristics are greatly improved as the acetyl content is increased from ca 20% (DS(acetyl) = 1) to ca 39% (DS(acetyl) = 2.4) (9).

The bulk density of cellulose acetate varies with physical form from 160 kg m⁻³ (10 lb ft⁻³) for soft flakes to 481 kg m⁻³ (30 lb ft⁻³) for hammer-milled powder, whereas the specific gravity (1.29–1.30), refractive index (1.48), and dielectric constant of most commercial cellulose acetates are similar.

In fibers, plastics, and films prepared from cellulose esters, mechanical properties such as tensile strength, impact strength, elongation, and flexural strength are greatly affected by the degree of polymerization and the degree of substitution. Mechanical properties significantly improve as the DP is increased from ca 100 to 250 repeat units.

Liquid Crystalline Solutions. Cellulose esters, when dissolved in the appropriate solvents at the proper concentration, show liquid crystalline characteristics similar to those of other rigid chain polymers (10) because of an ordered arrangement of the polymer molecules in solution. Cellulose triacetate dissolved at 30–40 wt % in trifluoroacetic acid, dichloroacetic acid, and mixtures of trifluoroacetic acid and dichloromethane exhibits brilliant iridescence, high optical rotation, and viscosity–temperature profiles characteristic of typical anisotropic phase-containing liquid crystalline solutions (11). Similar observations have been made for cellulose acetate butyrate (12), cellulose diacetate (13), and other cellulose derivatives (14,15). Wet spinning of these liquid crystalline solutions yields fibers with much higher strength properties than fibers normally obtained from cellulose esters (16,17).

Manufacture and Processing

Simple triesters such as cellulose formate [9036-95-7] (7), cellulose propionate [9004-48-2] (9,18), and cellulose butyrate [9015-12-7] (19) have been prepared and their properties studied; none of these triesters is produced in large quantities. Cellulose formate esters, prepared by reaction of cellulose with formic acid, are thermally (20) and hydrolytically (7) unstable. Cellulose propionate and cellulose butyrate triesters are synthesized by methods similar to those used in the preparation of cellulose acetate with propionic or butyric anhydride in the presence of an acid catalyst (21). These anhydrides, especially butyric, react more slowly with cellulose than acetic anhydride. Therefore, the cellulose must be activated and the temperature must be controlled to avoid degradation. Esterification rates decrease with increasing acyl chain length, and degradation becomes more severe in the order acetic < propionic < butyric < isobutyric anhydride. Esterification with isobutyric anhydride is normally so slow that highly activated cellulose must be used and the sulfuric acid catalyst must be distributed uniformly. Swelling agents, eg, water, containing dissolved acid catalyst are used to ensure uniform catalyst distribution for the preparation of isobutyrate esters. The swelling agent is removed by solvent exchange, leaving sorbed acid uniformly distributed in the activated cellulose (22).

Cellulose activated with ethylenediamine [107-15-3] is used to prepare high molecular-weight cellulose butyrate (23). Cellulose so activated has a larger measured surface area (120 m² g) than cellulose activated with acetic acid (4.8 m² g). The diamine is removed with water, followed by solvent exchange with acetic acid and butyric acid before esterification.

More recently, however, a process for the manufacture of ultrahigh molecular-weight cellulose esters has been developed by reaction of nonactivated, secondary cellulose with trifluoroacetic acid, trifluoroacetic anhydride, and either an organic acid or acid chloride (24). This process is amenable to a larger variety of organic esters not normally available through conventional means. The technique requires less reaction time, less excess solvent, and it is easier to control the extent of the reaction than conventional sulfuric acid activation. Unfortunately, the handling and toxic nature of trifluoroacetic acid and the anhydride currently prevent its use on a large scale.

Cellulose valerates have been synthesized by conventional methods using valeric anhydride and sulfuric acid catalyst (25,26). Alternatively, the cellulose is activated by soaking in water, which is then displaced by methylene chloride or valeric acid; the temperature is maintained at <38°C to minimize degradation.

Production of cellulose esters from aromatic acids has not been commercialized because of unfavorable economics. These esters are usually prepared from highly reactive regenerated cellulose, and their physical properties do not differ markedly from cellulose esters prepared from the more readily available aliphatic acids. Benzoate esters have been prepared from regenerated cellulose with benzoyl chloride in pyridine–nitrobenzene (27) or benzene (28). These benzoate esters are soluble in common organic solvents such as acetone or chloroform. Benzoate esters, as well as the nitrochloro-, and methoxy-substituted benzoates, have been prepared from cellulose with the appropriate aromatic acid and chloroacetic anhydride as the impelling agent and magnesium perchlorate as the catalyst (29).

Cellulose chloroacetates (30) and aminoacetates (30,31), acetate sorbates (32), and acetate maleates (33) have been prepared but are not commercially important. These esters are made from hydrolyzed cellulose acetate with the appropriate anhydride or acid chloride in pyridine.

Cellulose esters of unsaturated acids, such as the acetate methacrylate, acetate maleate (34), and propionate crotonate (35), have been prepared. They are made by treating the hydrolyzed acetate or propionate with the corresponding acyl chloride in a pyridine solvent. Cellulose esters of unsaturated acids are cross-linkable by heat or uv light; solvent-resistant films and coatings can be prepared from such esters.

Amine-containing cellulose esters, eg, the acetate *N,N*-diethylaminoacetate (36) and propionate morpholinobutyrate (35), are of interest because of their unique solubility in dilute acid. Such esters are prepared by the addition of the appropriate amine to the cellulose acrylate crotonate esters or by replacement of the chlorine on cellulose acrylate chloroacetate esters with amines. This type of ester has been suggested for use in controlled release, rumen-protected feed supplements for ruminants (36,37).

Mixed esters, such as cellulose acetate propionate and cellulose acetate butyrate, have desirable properties not exhibited by the acetate or the high acyl triesters. These mixed esters are produced commercially in multiton quantities by methods similar to those for cellulose acetate; they are prepared over a wide range of acyl substitutions and viscosities. The ratio of acetyl to higher acyl in the product is proportional to the concentration of components in the esterification solution (Figs. 5 and 6). Thus it is possible to esterify cellulose with propionic or butyric anhydride in the presence of acetic acid to produce the mixed esters. In a similar manner, acetic anhydride can be used in the esterification with either propionic or butyric acid to produce a cellulose ester containing both acyl moieties. The commercial production of cellulose acetate butyrate has been described (38), and the different reactivities of lower anhydrides toward cellulose have been investigated in detail. Cellulose butyrate has been prepared in homogenous solution by the reaction of cellulose in dimethyl sulfoxide (DMSO)-paraformaldehyde with butyric anhydride and pyridine catalyst (39). The maximum degree of substitution is ca 1.8, and the products are soluble in common organic solvents. Dichloromethane has been used in the preparation of cellulose acetate butyrate to prevent excessive

degradation and provide an ester with higher molecular weight (40).

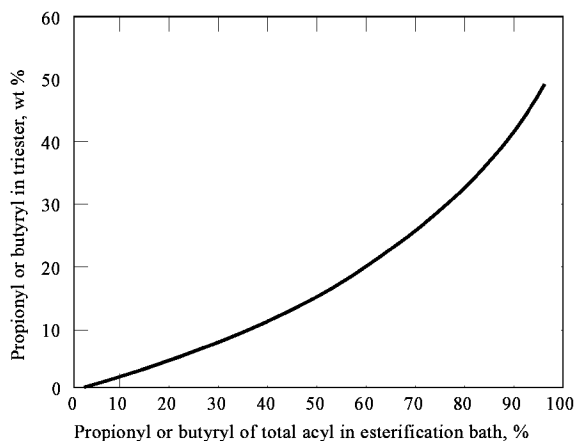


Fig. 5. Composition of cellulose acetate butyrate (propionate) as a function of butyryl (propionyl) content of esterification bath.

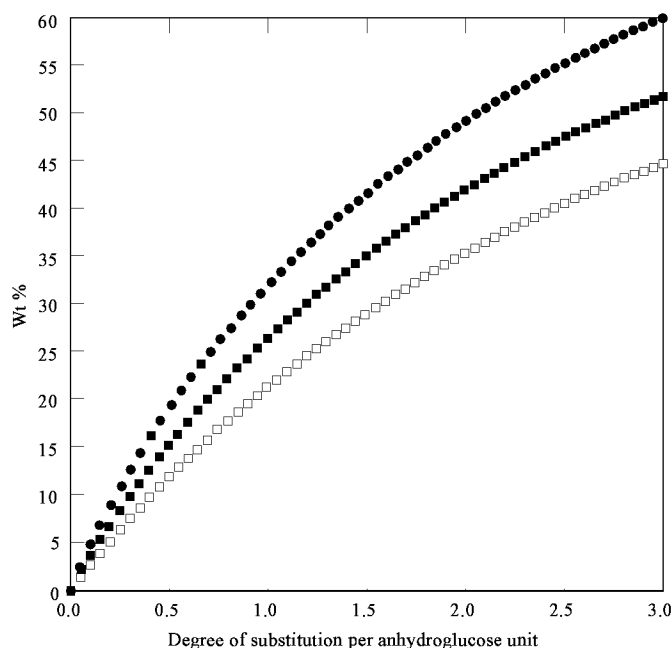


Fig. 6. Conversion of weight percent to degree of substitution per anhydroglucose unit (max = 3.0), where ● is butyryl, ◆ is propionyl, and ◇ is acetyl.

Mixed esters containing the dicarboxylate moiety, eg, cellulose acetate phthalate, are usually prepared from the partially hydrolyzed lower aliphatic acid ester of cellulose in acetic acid solvent by using the corresponding dicarboxylic acid anhydride and a basic catalyst such as sodium acetate (41,42). Cellulose acetate succinate and cellulose acetate butyrate succinate are manufactured by similar methods as described in reference 43.

Other mixed esters, eg, cellulose acetate valerate [55962-79-3], cellulose propionate valerate [67351-41-1], and cellulose butyrate valerate [53568-56-2], have been prepared by the conventional anhydride sulfuric acid methods (25). Cellulose acetate isobutyrate [67351-38-6] (44) and cellulose propionate isobutyrate [67351-40-0] (45) have been prepared with a zinc chloride catalyst. Large amounts of catalyst and anhydride are required to provide a soluble product, and special methods of delayed anhydride addition are necessary to produce mixed esters containing the acetate moiety. Mixtures of sulfuric acid and perchloric acid are claimed to be effective catalysts for the preparation of cellulose acetate propionate in dichloromethane solution at relatively low temperatures (46); however, such acid mixtures are considered too corrosive for large-scale productions.

Mixed esters are hydrolyzed by methods similar to those used for hydrolyzing cellulose triacetate. The hydrolysis eliminates small amounts of the combined sulfate ester, which, if not removed, affects thermal stability. Sulfuric acid is the preferred catalyst for hydrolysis since it is already present in the esterification mixture. On a large scale, partial neutralization of the catalyst may be necessary before hydrolysis. Increasing the amount of water during hydrolysis reduces the rates of viscosity reduction and acyl hydrolysis of cellulose acetate propionate and acetate butyrate esters (47). Several methods of hydrolyzing cellulose esters of higher aliphatic acids are described (48,49). Acetate phthalate mixed esters preferentially lose acetyl groups when hydrolyzed in aqueous acetic acid media with sulfuric acid catalyst. On the other hand, hydrolysis with a basic catalyst such as sodium or potassium acetate in aqueous acetic acid results in preferential loss of the phthaloyl moiety (50). Ester properties can be modified by changing the DS, ie, removing acyl groups.

Stabilization. After hydrolysis, precipitation, and thorough washing of the cellulose esters to remove residual acids, the esters must be stabilized against thermal degradation and color development, which may occur during processing, such as extrusion or injection molding. Thermal instability is caused by the presence of oxidizable substances and small amounts of free and combined sulfuric acid (51). The sulfuric acid combines with the cellulose almost quantitatively and most of it is removed during the latter stages of hydrolysis. The remaining sulfuric acid can be neutralized with alkali metal salts, such as sodium, calcium, or magnesium acetate, to improve ester stability. The combined sulfate ester may also be removed by treatment in boiling water or at steam temperatures in an autoclave. Treatment with aqueous potassium or calcium iodide reportedly stabilizes the cellulose acetate against thermal degradation (52).

Dialkyl esters of 3,3'-thiodipropionic acid (53), cyclic phosphonites such as neopentylphenyl phosphite, derivatives of phosphaphenathrene-10-oxide (54), secondary aromatic amines, eg, diphenylamine (55), and epoxidized soybean oils (56) are effective stabilizers for preventing discoloration of cellulose esters during thermal processing.

Exposure to uv radiation may cause chain scission and loss of physical properties in cellulose esters exposed to outdoor environments; esters formulated for such use must be stabilized accordingly. Some resorcinol and benzophenone derivatives, such as resorcinol monobenzoate and 2-hydroxy-4-methoxybenzophenone, are reportedly excellent uv-light stabilizers for cellulose esters (57,58). Other stabilizers include piperidine derivatives (59) and substituted triazole compounds alone (60) and in combination with resorcinol monobenzoate (61).

Cellulose Acetate. Almost all cellulose acetate, with the exception of fibrous triacetate, is prepared by a solution process employing sulfuric

acid as the catalyst with acetic anhydride in an acetic acid solvent. The acetylation reaction is heterogeneous and topochemical wherein successive layers of the cellulose fibers react and are solubilized in the medium, thus exposing new surfaces for reaction. The reaction course is controlled by the rates of diffusion of the reagents into the cellulose fibers, and therefore the cellulose must be swollen or activated before acetylation to achieve uniform reaction and avoid unreacted fibers in the solution (62).

Cellulose dissolved in suitable solvents, however, can be acetylated in a totally homogeneous manner, and several such methods have been suggested. Treatment in dimethyl sulfoxide (DMSO) with paraformaldehyde gives a soluble methylol derivative that reacts with glacial acetic acid, acetic anhydride, or acetyl chloride to form the acetate (63). The maximum degree of substitution obtained by this method is 2.0; some oxidation also occurs. Similarly, cellulose can be acetylated in solution with dimethylacetamide–paraformaldehyde and dimethylformamide-paraformaldehyde with a potassium acetate catalyst (64) to provide an almost quantitative yield of hydroxymethylcellulose acetate.

Several derivatives of cellulose, including cellulose acetate, can be prepared in solution in dimethylacetamide–lithium chloride (65). Reportedly, this combination does not react with the hydroxy groups, thus leaving them free for esterification or etherification reactions. In another homogeneous-solution method, cellulose is treated with dinitrogen tetroxide in DMF to form the soluble cellulose nitrite ester; this is then ester-interchanged with acetic anhydride (66). With pyridine as the catalyst, this method yields cellulose acetate with DS < 2.0.

In the fibrous acetylation process, part or all of the acetic acid solvent is replaced with an inert diluent, such as toluene, benzene, or hexane, to maintain the fibrous structure of cellulose throughout the reaction. Perchloric acid is often the catalyst of choice because of its high activity and because it does not react with cellulose to form acid esters. Fibrous acetylation also occurs upon treatment with acetic anhydride vapors after impregnation with a suitable catalyst such as zinc chloride (67).

An apparatus for the continuous fibrous acetylation of cellulose in benzene has been described (68,69). The process involves continuous activation, acetylation, partial saponification of the resulting triacetate, and drying of the product.

Activation of Cellulose. The activation required depends on the source of cellulose (cotton linter or wood pulp), purity, and drying history. Typical specifications for an acetylation-grade cellulose are given in Table 5. Cellulose that has never been dried or has been mildly dried to ca 5° moisture requires little, if any, further activation.

Table 5. Typical Specifications for Acetylation-Grade Pulp ^a

Property	Value
α-cellulose, min °	95.6
moisture, °	5.8 ^b
pentosans, max °	2.1
cuprammonium viscosity ^c , mPa·s(cP)	1100–4000
intrinsic viscosity, dL g	5.5–7.5
ether extractable, max °	0.15
ash, max °	0.08
iron, max ppm	10
trial acetylation	
haze, max ppm	100
color, max ppm	600

^a Ref. 62.
^b Off supplier's dryer.
^c 2.5° solution.

Normally, water or aqueous acetic acid is the activating agent; glacial acetic acid may also be used. Water is more effective because it swells the fibers more than other agents and alters the hydrogen bonding between the polymer chains to provide a greater surface area for reaction. When water or aqueous acids are used, the cellulose must be dehydrated by displacing the water with acetic acid before the start of acetylation. Commercially, it is not unusual to activate cellulose with glacial acetic acid containing a small part of the total required sulfuric acid catalyst; this reduces the molecular weight of the cellulose as needed to obtain a satisfactory product. The efficiency of activation is increased by increased temperature, time, amount of catalyst, and lower acetic acid–cellulose ratio. Several other swelling agents and methods for cellulose activation have been reported but have little commercial value because of cost and performance considerations.

Ethylenediamine (70,71), benzyl alcohol and acetone (72), ethylene glycol (73) and C₂–C₁₈ carboxylic acids (74) are claimed to increase the reactivity of cellulose toward acetylation. Sodium hydroxide and liquid ammonia (71) are excellent swelling agents and have been used to activate cellulose before esterification. Ultrasonic treatment of cellulose slurries (75) reportedly swells the fibers and improves reactivity.

In one process to produce highly activated cellulose for acetylation, cellulose is treated with NaOH (mercerization) followed by a hydroxyalkylating agent, eg, ethylene oxide or propylene oxide, to give a cellulose hydroxyalkyl ether with a DS of 0.05–0.3 (76). The resulting water-insoluble material is highly reactive to conventional acetic anhydride–sulfuric acid acetylation.

Catalysts for Acetylation. Sulfuric acid is the preferred catalyst for esterifying cellulose and is the only known catalyst used commercially for this function. The role of sulfuric acid during acetylation has been discussed (77,78). In the presence of acetic anhydride, sulfuric acid rapidly and almost quantitatively forms the cellulose sulfate acid ester (77). Even in the absence of anhydride, the sulfuric acid is physically or mechanically retained (sorbed) on the cellulose. The degree of absorption is a measure of the reactivity or accessibility of different celluloses.

Sulfuric acid reacts with acetic anhydride to form acetylsulfuric acid (79). This reaction is favored by low temperature and high anhydride concentration. In cellulose acetylation, probably both sulfuric acid and acetylsulfuric acid exist and react with cellulose to form cellulose sulfate acid ester.

Perchloric acid is a well-known acetylation catalyst, especially in the fibrous method of preparing cellulose triacetate. Unlike sulfuric acid, perchloric acid does not combine with cellulose (78), ie, it does not form esters, and therefore virtually complete acetylation (DS 3.0, 44.8° acetyl) occurs. However, the extremely corrosive nature of perchloric acid and explosive nature of its salts have precluded its use industrially as an acetylation catalyst.

Zinc chloride is a Lewis acid catalyst that promotes cellulose esterification. However, because of the large quantities required, this type of catalyst would be uneconomical for commercial use. Other compounds such as titanium alkoxides, eg, tetrabutoxytitanium (80), sulfate salts containing cadmium, aluminum, and ammonium ions (81), sulfamic acid, and ammonium sulfate (82) have been reported as catalysts for cellulose acetate production. In general, they require reaction temperatures above 50°C for complete esterification. Relatively small amounts (<0.5%) of sulfuric acid combined with phosphoric acid (83), sulfonic acids, eg, methanesulfonic, or alkyl phosphites (84) have been reported as good acetylation catalysts, especially at reaction temperatures above 90°C.

Hydrolysis. The primary functions of hydrolysis are to remove some of the acetyl groups from the cellulose triester and to reduce or remove the combined acid sulfate ester to improve the thermal stability of the acetate.

The acetylation reaction is stopped by the addition of water to destroy the excess anhydride, causing rapid hydrolysis of the combined sulfate acid ester (Fig. 7). This is followed by a much slower rate of hydrolysis of the acetyl ester groups. The rate of hydrolysis is controlled by temperature, catalyst concentration, and, to a lesser extent, by the amount of water. Higher temperatures and catalyst concentrations increase the rate of hydrolysis. Higher water content slightly increases the hydrolysis rate and helps minimize degradation (85). The amount of water also influences the ratio of primary to secondary

hydroxy groups in the hydrolyzed cellulose acetate; high water content favors primary hydroxyl formation (86).

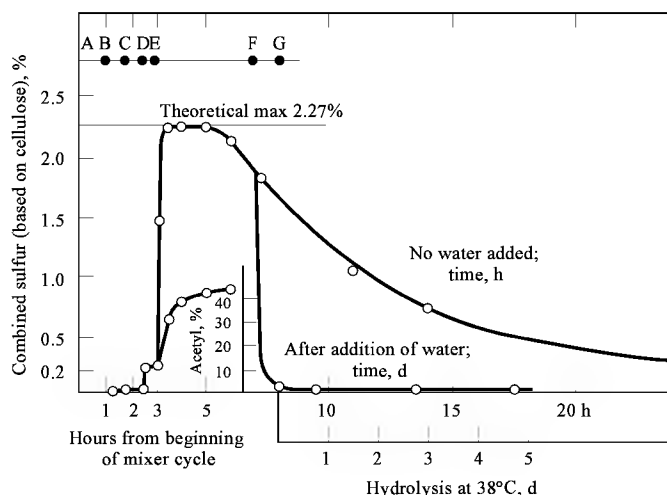


Fig. 7. Combined sulfur during preparation of cellulose acetate; hydrolysis of sulfate and esters (6). Acetylation schedule: A, mixer charged with linters and acetic acid; B, minor portion of catalyst added; C, began cooling to 18°C; D, acetic anhydride added and continued cooling to 16°C; E, significant portion of catalyst added; F–G, water added during 1 h.

In commercial processes, the water content during hydrolysis ranges from 5 to 20 wt % based on total liquids and depends on the temperature and the final product desired. Hydrolysis reactions can be performed at temperatures ranging from ca 38°C to pressurized reactions at 229°C (87). In a continuous process at 129°C, a triacetate solution is passed vertically upward through three consecutive chambers containing rotating disks to maximize plug flow of the solution (88). Kinetics of cellulose triacetate hydrolysis have been investigated (89) and, with sulfuric acid as the catalyst, the rate constant was found to be linear for both catalyst concentration and water content.

The rate of hydrolysis of cellulose acetate can be monitored by removing samples at intervals during hydrolysis and determining the solubility of the hydrolyzed acetate. When the desired DS is reached, the hydrolysis is stopped by neutralizing the catalyst with magnesium, calcium, or sodium salts dissolved in aqueous acetic acid.

Precipitation and Purification. During the hydrolysis, control tests are made by turbidimetric titration of samples taken intermittently. When the desired degree of hydrolysis is reached, the ester is precipitated from the reaction solution into water. It is important for the precipitate to have the proper texture for subsequent washing to remove acid and salts for thermal stabilization. Before precipitation, the reaction solution is usually diluted with additional aqueous acetic acid to reduce the viscosity. If a flake texture is desired, the solution is poured into a vigorously stirred, 10–15% aqueous acetic acid. To precipitate the acetate in powder form, dilute acetic acid is added to the stirred reaction solution. In both cases, the precipitated ester is suspended in 25–30% aqueous acid solutions and finally washed with deionized water. The dilution, precipitation temperature, agitation, and strength of the acid media must be controlled to ensure uniform texture.

Another method for direct precipitation of cellulose acetate powder suitable for extrusion into plastics is described (90). The reaction solution is precipitated with dilute aqueous acetic acid at 80–85°C in the presence of a coagulant such as isopropyl acetate. The resulting powder particles have a higher bulk density and absorb plasticizers more readily than powders obtained by the usual methods.

Granules can be precipitated and formed by extruding the viscous reaction mixture through a circular die containing several holes over which a knife blade rotates to cut the strands into granules (91). The granules are simultaneously slurried in dilute acetic acid to harden the particles for further washing.

Solution Process. With the exception of fibrous triacetate, practically all cellulose acetate is manufactured by a solution process using sulfuric acid catalyst with acetic anhydride in an acetic acid solvent. An excellent description of this process is given (85). In the process (Fig. 8), cellulose (ca 400 kg) is treated with ca 1200 kg acetic anhydride in 1600 kg acetic acid solvent and 28–40 kg sulfuric acid (7–10% based on cellulose) as catalyst. During the exothermic reaction, the temperature is controlled at 40–45°C to minimize cellulose degradation. After the reaction solution becomes clear and fiber-free and the desired viscosity has been achieved, sufficient aqueous acetic acid (60–70% acid) is added to destroy the excess anhydride and provide 10–15% free water for hydrolysis. At this point, the sulfuric acid catalyst may be partially neutralized with calcium, magnesium, or sodium salts for better control of product molecular weight.

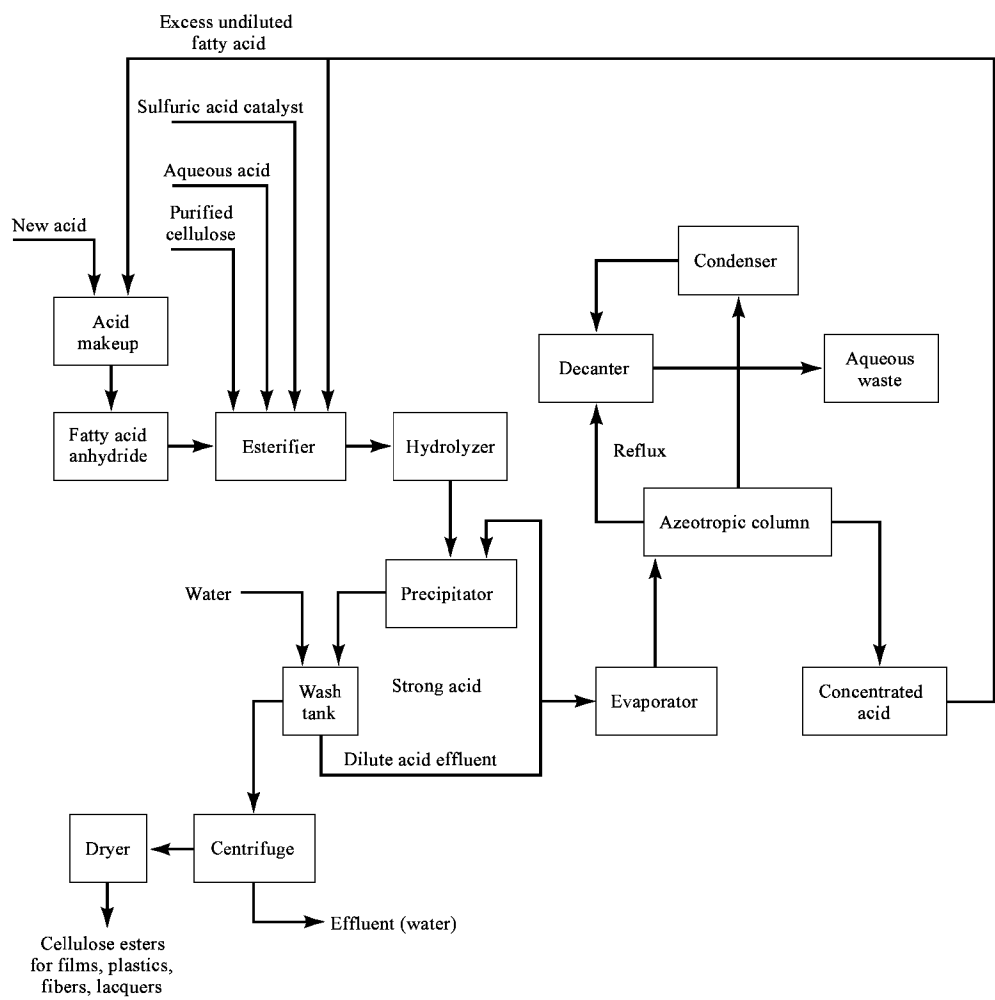


Fig. 8. Process flow sheet for cellulose esters.

The cellulose acetate is hydrolyzed in solution at 40–50°C for varying lengths of time (4–20 h) until the desired DS is obtained; at this point, the ester is precipitated with dilute aqueous acetic acid. The precipitate is hardened in 25–30° aqueous acetic acid, which is drained off and recovered.

The ester is washed thoroughly in iron-free water to remove acid and any desirable salts; these wash liquids are sent for acid recovery. The final wash may contain some sodium, calcium, or magnesium ions to stabilize traces of sulfate esters remaining on the cellulose acetate.

Recent Developments. A considerable amount of cellulose acetate is manufactured by the batch process, as described previously. In order to reduce production costs, efforts have been made to develop a continuous process that includes continuous activation, acetylation, hydrolysis, and precipitation. In this process, the reaction mixture, ie, cellulose, anhydride, catalyst, and solvent, pass continuously through a number of successive reaction zones, each of which is agitated (92,93). In a similar process, the reaction mass is passed through tubular zones in which the mixture is forced through screens of successively small openings to homogenize the mixture effectively (94). Other similar methods for continuous acetylation of cellulose have been described (95,96).

Cellulose acetate with improved solubility properties can be prepared from low quality wood pulps by multistage addition of the components (97) or by interrupting the reaction in the early stages, filtering, and continuing the acetylation with fresh reactants (98,99).

In an integrated continuous process, cellulose reacts with acetic anhydride prepared from the carbonylation of methyl acetate with carbon monoxide. The acetic acid liberated reacts further with methanol to give methyl acetate, which is then carbonylated to give additional acetic anhydride (100,101).

High temperature acetylation of cellulose above 50°C produces cellulose acetate from low purity wood pulp cellulose in shorter reaction times. In a high temperature method recently disclosed (102), cellulose reacts with 200–400° acetic anhydride in the presence of <5% acid catalyst at 68–85°C for 3–20 min. After the acid catalyst is neutralized with magnesium acetate, the cellulose acetate is hydrolyzed at 120°C for two hours (103). Several modified catalyst systems have been developed for acetylation of cellulose above 90°C (89,90).

Economic Aspects

From 1980 to 1988, annual cellulose acetate flake production in the United States showed a slight decrease in production from 392,000 t to 323,000 t with an annual decline of 0.4 to 0.1% (Table 6). World demand for cellulose acetate flake has also fallen. A modest recovery has occurred in recent years as a result of the increased demand for cigarette-filter tow; world consumption of cigarette-filter tow has risen about 2.5° per year since 1980 (Tables 7 and 8). In contrast, world demand for textile fibers and cellulose ester plastics decline 4.6° and 4.2° per year, respectively (Fig. 9).

Table 6. U.S. Consumption of Cellulose Acetate Flake,^a 10³ t

Year	Cigarette-filter tow	Textile fibers	Cellulose acetate plastics ^b	Total
1979	164	145	83	392
1980	175	145	48	368
1983	173	105	62	339
1988	205	68	50	323
1993	210–215	59	47	315–321
Average annual growth rate				
1988–1993	0.5–1.0°	3.0	1.1%	0.4–0.1%

^a Data are reported as cellulose acetate flake equivalents; plasticizers not included.

^b Mixed esters (CAB and CAP) included. Courtesy of CEH Estimates.

Table 7. World Consumption of Cellulose Acetate Flake,^a 10³ t

Year	Textile fibers	Cigarette-filter tow	Plastics ^b	Total
1980	335	338	132	805
1985	241	335	172	710
1987	240	401	98	740

^a Data for textile fibers and cigarette-filter tow include Eastern Europe and the People's Republic of China.
^b Cellulose acetate ester plastics are produced largely in the United States, Western Europe, and Japan. World consumption is assumed to be approximately equivalent to production of cellulose ester plastics in these three regions. Courtesy of CEH Estimates.

Table 8. World Capacity for Cellulose Acetate Flake, 1988, 10³ t

Region	Capacity
North America	
Canada	30
United States	453
Central America	
Mexico	20
Western Europe	
Belgium	12
France	25
Germany (formerly FRG)	25
Italy	9
Spain	2
United Kingdom	68
Eastern Europe	
Germany (formerly GDR)	6
Russia	70
Asia	
Japan	112
Totals ^a	832

^a In addition to the producers listed above, Victorio Ghisolfi with state owned Gepi purchased the Taban SpA (a Mon-tedison subsidiary) plant in Pallanza, Italy in 1988 with plans to restart in 1989 (4).
Courtesy of CEH Estimates.

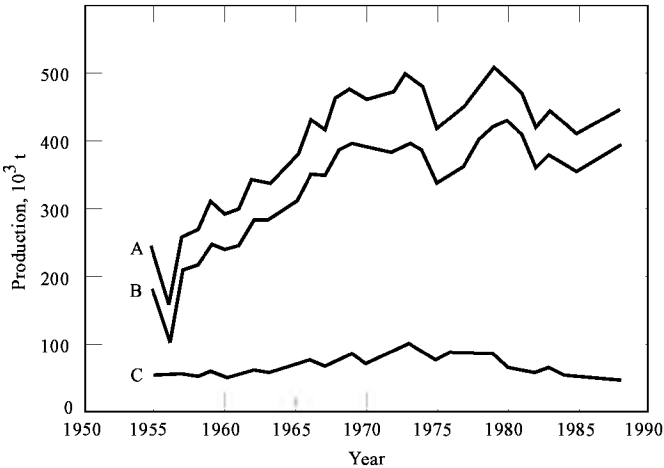


Fig. 9. U.S. production of cellulose esters; A, total cellulose esters production; B, cellulose acetate flake; C, other cellulose esters, ie, cellulose nitrate, cellulose acetate propionate, cellulose acetate butyrate (4).
Courtesy of CEH Estimates.

Demand for cellulose acetate flake in the United States is projected to decline slightly from 1988 to 1993. Cigarette-filter tow for export is the only market projected to grow. Cellulose acetate for textile fibers is expected to decline, as will flake demand for plastics, with the growth of photographic films somewhat offsetting declining markets in other plastics end uses.

The price of cellulose ester flake has generally increased with inflation and as of mid-1987 was estimated at ca \$3.64–\$4.71 kg for cellulose diacetate molding resin and from ca \$4.16–\$4.71 kg for the mixed esters molding resins depending on purity and the number of propionyl or butyryl esters (4).

From 1946 to mid-1987, Farbenfabriken Bayer AG in Germany was the European producer of cellulose acetate, cellulose acetate butyrate (CAB), and cellulose acetate propionate (CAP) before closing its facilities. Bayer's exit from the cellulose acetate mixed esters business leaves Eastman Chemical Co. in the United States as the sole producer of CAB-CAP resins.

In the United States, plastic and fiber grades of cellulose acetate and mixed cellulose ester flake, ie, acetate butyrate and acetate propionate, are produced by the Eastman Chemical Co.; Hoechst-Celanese manufactures a fiber-grade cellulose acetate flake suitable for plastics applications. Foreign producers of cellulose acetate flake include Gevaert and Fabelta in Belgium; Rh ne Poulenc Chemie in France; British Hercules, Courtaulds, and Nelson in the United Kingdom; Mazzucchelli Celluliodi SpA and Montedison in Italy; and Daicel and Teijin in Japan.

Cellulose ester flake production for nonfiber applications represents a small part of the total U.S. output. Cigarette-filter tow and cellulose acetate textile fibers consume more than 80% of flake production (104).

With the takeover of the American Celanese Corp. in mid-1986, the new Hoechst Celanese Corp., with Eastman Chemical Co. are the world leaders in cellulose acetate tow and flake production as of this writing. With confidence in both the acetate market and acetic anhydride supply (105), Hoechst

Celanese recently announced an expansion that will double its tow and flake capacity from 35,750 metric tons to 60,500 metric tons by 1994 (106). The increased capacity will be achieved through expansions and productivity improvements at the U.S., Belgium, Canada, Mexico, and China operation centers.

In a similar announcement, Eastman Chemical Co. and Rhône-Poulenc S.A. have recently formed a 50/50 joint venture to make 59,090 metric tons/yr of cellulose acetate filter tow and fiber by the fourth quarter of 1993 (107). Eastman Chemical Co. announced a multimillion dollar expansion of its own filter tow capacity by approximately 11,363 metric tons/yr to be completed by mid-1991. The expansion brings the company's worldwide filter tow capacity up to 154,545 metric tons (108). Eastman Chemical Co. announced plans to expand the production of cellulose acetate butyrates and cellulose acetate propionates by 20 and 40%, respectively, by mid-1991 (109).

Analytical and Test Methods

Standardized test methods for analyzing the chemical composition, viscosity, and physical properties of cellulose esters have been adopted by the ASTM and are described in substantial detail (110).

Degree of Substitution and DS Distribution. For cellulose esters, the substitution level is usually expressed in terms of DS; that is, the average number of substituents per anhydroglucose unit (AGU). Cellulose contains three hydroxyl groups in each AGU unit that can be substituted; therefore DS can have a value between zero and three. Because DS is a statistical mean value, a value of 1 does not assure that every AGU has a single substituent. In some cases there can be unsubstituted anhydroglucose units, some with two and some with three substituents, and more often than not the value will be a noninteger. The physical properties commonly associated with commercial cellulose acetates, cellulose acetate butyrates, and cellulose acetate propionates are, in many cases, directly related to the degree of substitution as well as the overall substitution pattern. The degree of substitution or acetyl content of cellulose acetate has traditionally been determined by saponifying a known amount of the ester with an excess of standard sodium hydroxide solution in the presence of swelling agent or solvent. The excess sodium hydroxide is back-titrated with a standard solution of hydrochloric acid to determine the total acetyl content. The relative amounts of acetyl, propionyl, and butyryl in cellulose mixed esters, however, are determined by partition analysis in butyl acetate–water mixtures. The esters are saponified in sodium hydroxide, and phosphoric acid is added to liberate the organic acids from their sodium salts. The acids are partitioned between butyl acetate and water and their mole ratios are determined by comparison to carefully prepared control standards.

The acetyl content of cellulose acetate may be calculated by difference from the hydroxyl content, which is usually determined by carbanilation of the ester hydroxy groups in pyridine solvent with phenyl isocyanate [103-71-9], followed by measurement of uv absorption of the combined carbanilate. Methods for determining cellulose ester hydroxyl content by near-infrared spectroscopy (111) and acid content by nmr spectroscopy (112) and pyrolysis gas chromatography (113) have been reported.

With the advent of high resolution proton and carbon nuclear magnetic resonance spectroscopy, however, determining the DS and the DS distribution of mixed ester systems by aqueous saponification has become obsolete. Numerous studies have shown nmr to be a fundamental tool for probing the microscopic behavior of a wide variety of synthetic polymers and biomacromolecules (114). In the past, however, most spectral assignments required laboriously prepared derivatives containing a trideuterioacetyl or trideuteriomethyl group at a predetermined position or by comparison to spectra of mono- or oligosaccharides (115). These methods proved to be limited in detail because of line broadening and small differences in chemical shifts. Understanding the basic relationships between macroscopic properties and the microstructure of these biopolymer derivatives through nmr is the direction of much cellulose esters research.

Determining the degree of substitution using standard proton nmr relies on the integral ratio between the cellulosic ring protons (≈ 5.0 – 2.9δ) and the ester alkyl protons ($\approx 1.2\delta$ for butyryl and propionyl and $\approx 2.0\delta$ for acetyl methyl groups). This simple procedure is used extensively to determine the extent of esterification and is currently the fastest, easiest way for determining the DS of mixed cellulose esters.

Standard proton nmr techniques provide information on the degree of substitution and ester ratios in mixed ester systems, but it has been the development of two-dimensional techniques that has allowed the greatest insight into the microstructure of the cellulosic polymer (116–119). The combination of ^1H and ^{13}C nmr spectroscopy has, for example, been applied to cellulose triacetate for determination of its configuration (120), identification of the chemical shifts of ring protons and carbons (117), and determination of the distribution of acetyl groups over C₂, C₃, and C₆ (118,121). More complex experiments such as insensitive nuclei assigned by polarization transfer (INAPT) and nuclear Overhauser exchange spectroscopy (NOESY) have been successfully applied toward the spectral assignments of most common triesters, the results of which are listed in Table 9. With INAPT, the lack of sensitivity that is commonly associated with two-dimensional nmr techniques is generally avoided. This increased sensitivity circumvents the need for ^{13}C enrichment and decreases the demand on instrument time.

Table 9. ^1H and ^{13}C Nmr Chemical Shifts, ppm, and Coupling Constants, J ,^a for Cellulose Triacetate, Cellulose Tripropionate, and Cellulose Tributurate^b

	CTA DMSO-d ₆ , 25°C	CTA DMSO-d ₆ , ^c	CTA CDX ₃ , ^d	CTP CDX ₃ , ^d , 25°C	CTB CDX ₃ , ^d , 25°C
	<i>¹H Values</i>				
H-1	4.65 (d, $J_{1,2}$ = 7.9 Hz)	4.65 (d, $J_{1,2}$ = 7.9 Hz)	4.42 (d, $J_{1,2}$ = 7.9 Hz)	4.35 (d, $J_{1,2}$ = 7.9 Hz)	4.65 (d, $J_{1,2}$ = 7.9 Hz)
H-2	4.52 (t, J = 7.3 Hz)	4.55 (t, J = 8.6 Hz)	4.79 (t, J = 8.6 Hz)	4.77 (t, J = 8.6 Hz)	4.76 (t, J = 8.6 Hz)
H-3	5.06 (t, J = 9.2 Hz)	5.04 (t, J = 9.2 Hz)	5.07 (t, J = 9.0 Hz)	5.07 (t, J = 9.1 Hz)	5.06 (t, J = 9.2 Hz)
H-4	3.65 (t, J = 9.2 Hz)	3.68 (t, J = 9.2 Hz)	3.71 (t, J = 9.2 Hz)	3.66 (t, J = 9.1 Hz)	3.61 (t, J = 9.2 Hz)
H-5	3.81 (m)	3.77 (m)	3.53 (m)	3.47 (m)	3.48 (m)
H-6	4.22 (d, $J_{6\text{a},6\text{r}}$ = 10 Hz)	4.26 (d, $J_{6\text{a},6\text{r}}$ = 10 Hz)	e	e	e
H-6 _r	3.98 (m)	4.04 (m)	4.06 (m)	4.03 (m)	4.03 (m)
	<i>¹³C Values</i>				
C-1		99.8 (d, J = 167 Hz)	100.4 (d, J = 165 Hz)	100.3 (d, J = 163 Hz)	100.1 (d, J = 163 Hz)
C-2		72.2 (d, J = 152 Hz)	71.7 (d, J = 153 Hz)	71.7 (d, J = 150 Hz)	71.4 (d, J = 150 Hz)
C-3		72.9 (d, J = 151 Hz)	72.5 (d, J = 148 Hz)	72.2 (d, J = 148 Hz)	71.8 (d, J = 147 Hz)
C-4		76.4 (d, J = 151 Hz)	76.0 ^f	75.8 (d, J = 153 Hz)	75.8 ^f
C-5		72.5 (d, J = 146 Hz)	72.7 (d, J = 139 Hz)	73.0 (d, J = 138 Hz)	73.1 (d, J = 143 Hz)
C-6		62.8 (t, J = 151 Hz)	61.9 (t, J = 151 Hz)	61.9 (t, J = 147 Hz)	61.9 (t, J = 145 Hz)
C-2 acetyl			169.1 ^g		
C-3 acetyl			169.6 ^g		
C-6 acetyl			170.7 ^g		

^a Digital resolution for ^1H was 0.20–0.26 Hz; For additional information see Ref. 116. For ^{13}C the digital resolution was 0.52 Hz.

^b All solutions are 30 mg/mL.

^c At 80°C for ^1H ; and 90°C for ^{13}C .

^d X = Cl for ^1H ; X = I for ^{13}C . 25°C

^e H-6_r overlaps with H-1.

^f The coupled resonance overlaps with the solvent peaks. For additional information see Refs. 116 and 117.

^g Doublet, coupling constant unavailable.

Other two-dimensional techniques, such as COSY (122), DEPT (123), HOHAHA, solid state (124) etc. give varying degrees of success when applied to the structure-property relationship of cellulose triesters. The recent application of ^1H - ^{13}C multiple-bond correlation (HMBC) spectroscopy for the unambiguous assignment of cellulose mixed esters has successfully demonstrated the utility of nmr for the structure elucidation of complex cellulose esters (125). It is this unique ability to provide detailed information on intermolecular interactions of cellulose esters in coatings (119) or in polymeric blends that continues to put nmr spectroscopy well ahead of other analytical techniques.

Viscosity. The viscosity of cellulose esters, a measure of the degree of polymerization, is determined by the falling-ball method. The time in Saybolt units (SU) required for an aluminum or stainless-steel ball of specified diameter to go through a specified distance in a solution of the cellulose ester is determined. The choice of solvents used to prepare the solutions for viscosity determination depends on the DS of the cellulose ester; the concentration of ester in the solution is normally 20 wt %. Dilute-solution viscosity (intrinsic viscosity) is determined by using a solution of 0.25-g ester dissolved in 100 mL of solvent. The flow time of the solution through a specially designed capillary viscometer is compared to that of the pure solvent. Methods of calculating molecular weight from intrinsic viscosity of cellulose esters have been reported (126).

Thermal Properties. The thermal stability of cellulose esters is determined by heating a known amount of ester in a test tube at a specific temperature a specified length of time, after which the sample is dissolved in a given amount of solvent and its intrinsic viscosity and solution color are determined. Solution color is determined spectroscopically and is compared to platinum-cobalt standards. Differential thermal analysis (dta) has also been reported as a method for determining the relative heat stability of cellulose esters (127).

The thermal transitions of a cellulose ester such as the glass-transition temperature and the melting point are usually determined by differential scanning calorimetry (dsc) (Fig. 10), which measures the flow of heat into and out of a sample. Generally a first heating run is necessary in order to erase any previous thermal processing characteristics, ie, regions of crystallinity. A slow cool followed by a reheat above the melt temperature provides information on the glass-transition temperature, crystallization temperature (exothermic), and the melting temperature (endothermic). This information is essential for the development of new thermoplastics.

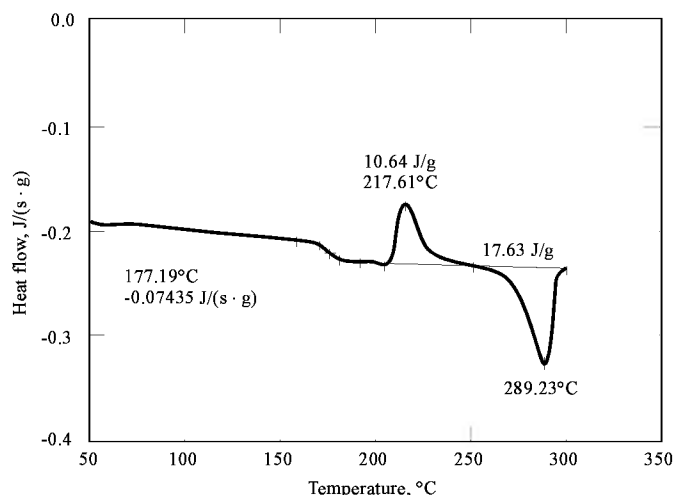


Fig. 10. Differential scanning calorimetry of cellulose triacetate. Second heating at $20^\circ\text{C min}^{-1}$; glass-transition (T_g) temperature 177°C ; crystallization on heating (T_{ch}) 217°C ; melting temperature (T_m) 289°C . To convert J to cal, divide by 4.184.

Similar information can be obtained from analysis by dynamic mechanical thermal analysis (dmta). Dmta measures the deformation of a material in response to vibrational forces. The dynamic modulus, the loss modulus, and a mechanical damping are determined from such measurements. Detailed information on the theory of dmta is given (128).

Determination of the thermal decomposition temperature by thermal gravimetric analysis (tga) defines the upper limits of processing. The tga for cellulose triacetate is shown in Figure 11. Comparing the melt temperature (289°C) from the dsc in Figure 10 to the onset of decomposition in Figure 11 defines the processing temperature window at which the material can successfully be melt extruded or blended.

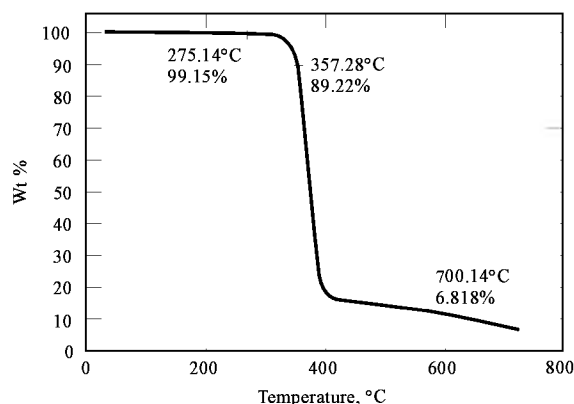


Fig. 11. Thermogravimetric analysis of cellulose triacetate. Method: $20^\circ\text{C min}^{-1}$ to 700°C , in (N_2) at 40 mL min^{-1} purging rate.

Molecular Weight. The molecular-weight distribution of cellulose esters is normally determined by gel-permeation chromatography (129) in which the ester, dissolved in a suitable solvent, is eluted through a column of porous cross-linked polystyrene. The elution profiles are compared to narrow molecular-weight polystyrene standards to obtain the molecular weight or DP distribution. Other methods, such as fractional precipitation and fractional extraction, although considerably more laborious, may be used to determine DP and DS distribution of cellulose esters (130). The DP of cellulose triacetate has been determined by gpc using a styrene-divinylbenzene copolymer column with an assigned peak molecular weight of approximately 60,000. Other solvents such as THF and NMP have also been shown to solvate secondary cellulose acetates and mixed esters for gpc analysis (131).

Health and Safety Factors

The vapors of the organic solvents used in the preparation of cellulose ester solutions represent a potential fire, explosion, or health hazard. Care should be taken to provide adequate ventilation to keep solvent vapor concentrations below the explosive limits. Mixing equipment should be designed to ensure that solvent temperatures do not approach their flash point during the mixing cycle. All equipment must be electrically grounded to prevent static discharge, and appropriate precautions should be followed as recommended by the manufacturer of the solvents.

Mixing cellulose esters in nonpolar hydrocarbons, such as toluene or xylene, may result in static electricity buildup that can cause a flash fire or explosion. When adding cellulose esters to any flammable liquid, an inert gas atmosphere should be maintained within the vessel (132). This risk may be reduced by the use of conductive solvents in combination with the hydrocarbon or by use of an antistatic additive. Protective clothing and devices should be provided.

Cellulose esters, like most dry organic materials in powder form, are capable of creating dust explosions (133). The explosion at Bayer's cellulose acetate plant at Dormagen, Germany in 1976 can attest to the explosive potential of dust. Damage to the plant was estimated at between DM 5–10 million (134).

Cellulose esters are considered nontoxic and may be used in food-contact applications. However, since cellulose esters normally are not used alone, formulators of coatings and films for use in food packaging should ensure that all ingredients in their formulations are cleared by the United States Food and Drug Administration for such use.

Uses

The cellulose esters with the largest commercial consumption are cellulose acetate, including cellulose triacetate, cellulose acetate butyrate, and cellulose acetate propionate. Cellulose acetate is used in textile fibers, plastics, film, sheeting, and lacquers. The cellulose acetate used for photographic film base is almost exclusively triacetate; some triacetate is also used for textile fibers because of its crystalline and heat-setting characteristics. The critical properties of cellulose acetate as related to application are given in Table 10.

Table 10. Uses and Critical Properties of Cellulose Acetate^a

Property	Use ^b			
	Yarn	Photographic film	Plastics	Lacquers
color, absence of haze	I		C	I
false viscosity ^c	I	I	I	I
filterability	C	I	I	I
adhesion		C		
radioactive contamination				

^a Ref. 62.
^b I = important; C = critical.
^c Concentrated solution viscosity higher than predicted for the intrinsic viscosity.

Large quantities of secondary cellulose acetate are used worldwide in the manufacture of filter material for cigarettes. Because of its excellent clarity and ease of processing, cellulose acetate film is widely used in display packaging and extruded plastic film for decorative signs (see PACKAGING MATERIALS). Injection-molded plastics of cellulose acetate are used in toothbrush handles, computer brushes, and a large variety of other applications (7).

Low viscosity cellulose acetate is used in lacquers and protective coatings for paper, metal, glass, and other substrates and as an adhesive for cellulose photographic film because of its quick bonding rate and excellent bond peel strength (135) (see COATINGS). Heat-sensitive adhesives for textiles have also been prepared from cellulose acetate (136). Extruded cellulose acetate film makes an excellent base for transparent pressure-sensitive tape (137) (see ADHESIVES).

Cellulose acetate films, specially cast to have a dense surface and a porous substructure, are used in reverse osmosis to purify brackish water (138–141) in hollow fibers for purification of blood (artificial kidney) (142), and for purifying fruit juices (143,144) (see MEMBRANE TECHNOLOGY).

Compaction of cellulose acetate desalination membranes, causing reduction in throughput and performance with time, can be significantly reduced by irrigation grafting of styrene onto the membrane (145).

Eyeglass frames made of cellulose acetate plasticized with diglycerol esters do not exhibit opaqueness at the frame-lens junction with polycarbonate plastic lenses (146,147).

Biodegradable film (148), foam-molding compositions, eg, sponges (149), tobacco substitutes (150), and microencapsulated drug-delivery systems (151) are potentially new and useful applications for cellulose acetate esters.

With the renewed interest in environmentally friendly products, cellulose esters are being re-evaluated as a natural source of biodegradable thermoplastics. Cellulose acetates are potentially biodegradable (152). Films prepared from a cellulose acetate with a DS of 2.5 were shown to require only a 10–12 day incubation period for extensive degradation in an *in vitro* enrichment assay. Similarly, films prepared from a cellulose acetate with a DS of 1.7 saw 70% degradation in 27 days in a wastewater treatment facility, whereas films prepared from a cellulose acetate with a DS of 2.5 required approximately 10 weeks for similar degradation to occur. The results of this work demonstrate that cellulose acetate fibers and films are potentially environmentally nonpersistent.

Cellulose acetate propionate and butyrate esters have numerous applications, such as sheeting, molding plastics, film products, lacquer coatings, and melt dip coatings. The properties of propionate and acetate propionate esters ordinarily lie between those of cellulose acetate and acetate butyrate. The acetate propionate mixed esters have traditionally covered a narrow composition range compared to the range of acetate butyrate esters. Table 11 shows uses and a range of commercial compositions of cellulose acetate butyrate esters. Through proper variation of acetyl and butyryl contents, the esters can be adapted to a broad range of applications. Cellulose acetate propionate and acetate butyrate are thermoplastic; properly formulated, these esters are processible by methods such as injection molding and extrusion and can be dissolved and cast into films from a variety of solvents (see FILMS). The mixed esters are generally more compatible with various plasticizers and synthetic resins than the acetates, and their films possess excellent clarity and toughness. For example, cellulose acetate butyrate is compatible with polyester, acrylic, vinyl, and alkyd resins (qv), depending on the amount of butyryl substitution and the degree of hydrolysis of the esters.

Table 11. Application and Characteristics of Commercial-Grade Cellulose Acetate Butyrate^a

Acetyl, %	Butyryl, %	Hydroxyl, %	Degree of esterification ^b		Hydroxyl	Application
			Acetate	Butyrate		
29.5	17	1	2.1	0.7	0.2	lacquers
20.5	26	2.5	1.4	1.1	0.5	lacquers
13	37	2	0.95	1.65	0.4	plastics, lacquers

6	48	1	0.5	2.3	0.2	melt coatings
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^a Ref. 153.
Courtesy of Chapman and Hall.

^b Ratio of ester groups to glucose residues (see Fig. 6).

Cellulose acetate butyrates with high butyryl content and low viscosity are soluble in inexpensive lacquer solvents. They are widely used in lacquers for protective and decorative coatings applied to automobiles and wood furniture.

Higher butyryl esters, formulated with acrylic polymers, provide coatings with excellent weather resistance, good colorfastness and dispersibility, and good flow properties (154). Formulations for a typical automotive refinishing lacquer and a wood furniture lacquer are given in Tables 12 and 13, respectively. Low viscosity, high butyryl cellulose esters tolerate substantial amounts of alcohol solvent without appreciable increase in solution viscosity. An alcohol-soluble cellulose acetate butyrate containing ca 50° 0 butyryl and ca 4.5° 0 hydroxy is available commercially.

Table 12. CAB–Polyester Automotive Refinishing Lacquer^a

Components	Wt ° 0
polyester	11.5
CAB 381-20 ^b	11.4
CAB 381-0.5 ^b	5.7
phosphoric acid, 85° 0	0.3
TiO ₂ pigment	4.2
toluene	34.4
xylene	6.1
MIBK	5.0
isopropyl alcohol	9.3
acetone	7.5
<i>n</i> -butyl alcohol	3.2
Ektasolve EB acetate ^c	1.4
<i>Total</i>	<i>100.0</i>

^a Ref. 154.
^b CAB = cellulose acetate butyrate.
^c Eastman Kodak Co.

Table 13. CAB-Based Clear Topcoat Formulation for Wood Furniture

Components	Wt ° 0
CAB ester ^a	16.1
Unirez 7003 maleic resin ^b	17.4
DOP ^c	4.0
toluene	35.3
isopropyl alcohol	14.0
acetone	4.5
xylene	7.7
SF-69 ^d	1.0
<i>Total</i>	<i>100.0</i>

^a CAB = cellulose acetate butyrate.
^b Union Camp Corp.
^c DOP = dioctyl phthalate.
^d Slip aid; 1° 0 xylene (General Electric Co.)

Low viscosity cellulose propionate butyrate esters containing 3–5° 0 butyryl, 40–50° 0 propionyl, and 2–3° 0 hydroxyl groups have excellent compatibility with oil-modified alkyd resins (qv) and are used in wood furniture coatings (155). Acetate butyrate esters have been used in such varied applications as hot-melt adhesive formulations (156), electrostatically spray-coated powders for fusible, non-cratering coatings on metal surfaces (157–159), contact lenses (qv) with improved oxygen permeability and excellent wear characteristics (160–162), and as reverse-osmosis membranes for desalination of water (163).

In a relatively new decorative-coating technique called wet-on-wet coatings, cellulose acetate butyrate ester as the pigmented basecoat provides good pigment and metal-flake control before applications of the clear topcoat (164,165). Such coatings provide good appearance and excellent resistance to weathering and are expected to find broad use in automotive decorative coatings.

Because of certain properties, such as a high melting point, high tolerance for alcohol solvents, low odor, and excellent surface hardness, cellulose acetate propionates are used in printing inks (flexographic and gravure) (166) (Table 14). Alcohol-soluble cellulose acetate propionate ester tolerates substantial quantities of water in the solvent blend and thus provides an environmentally desirable system for flexographic ink coatings (167).

Table 14. Flexographic Ink Formulation Containing Alcohol-Soluble Cellulose Acetate Propionate

Components	Wt ° 0
cellulose acetate propionate ^a	6.1
sucrose acetate isobutyrate (SAIB)	1.5
Kodaflex DOP plasticizer ^b	4.1
Uni-Rez 710 maleic resin ^c	8.2
pigment	5.1

isopropyl alcohol, 99° o ^a	56.3
water	18.7
<i>Total</i>	<i>100.0</i>

^a Alcohol-soluble propionate (ASP) CAP 504-0.2.

^b DOP dioctyl phthalate (Eastman Kodak Co.)

^c Union Camp Corp.

Acetate propionate esters are nontoxic, exhibit excellent clarity and high tensile strength, and can be formulated into hot-melt dip coatings for food (168). Alternatively, they may be dissolved in volatile solvents and applied to foods in the form of a lacquer coating (169). Desalination membranes with improved, rigid, and stable surfaces have been prepared from cellulose acetate propionate (170). These films are generally more resistant to hydrolysis than those from cellulose acetate. Cellulose esters, especially acetate propionate and acetate butyrate mixed esters, have found limited use in a wide variety of specialty applications such as in nonfogging optical sheeting (171), low profile additives to improve the surface characteristics of sheet-molding (SMC) compounds and bulk-molding (BMC) compounds (172,173), and controlled drug release via encapsulation (174).

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INORGANIC ESTERS

Cellulose esters are cellulose derivatives that result from the esterification of the free hydroxyl groups of cellulose with one or more acids. The esterification can be achieved using mineral acids as well as organic acids or their anhydrides (see CELLULOSE ESTERS, ORGANIC). Cellulose nitrate [9004-70-0] (CN) is the oldest cellulose derivative and the only inorganic ester of commercial importance (1–5). CN was first prepared by Braconnot (6) in 1832. Schonbein (7) first developed the preferred method of manufacturing CN using HNO₃–H₂SO₄ mixtures. Subsequently, Abel (8) developed a method of safely handling CN. This process allowed CN to achieve military importance for its use as an explosive, eg, gun cotton. CN was later combined with camphor to produce the first successful synthetic thermoplastic, celluloid (9). Currently, lacquer finishes constitute the largest market for CN; explosives and propellants are the second largest market.

Other inorganic esters of cellulose have been frequently described and investigated. However, only CN has achieved any commercial significance.

Sulfur-Containing Cellulose Esters. Cellulose dissolves in 70–75% of sulfuric acid and a highly degraded, thermally unstable cellulose sulfate [9032-43-3] (CS) can be obtained from a sufficiently aged solution by precipitation (10,11). A maximum degree of substitution (DS) of 1.5 has been achieved by this process. Numerous attempts have been made to find better methods of preparing water-soluble cellulose sulfate. The currently known systems have been outlined by Klug (12). The reaction of cellulose with sulfuric acid in C₃–C₅ alcohols, and inert organic solvents, yields water-soluble CS without severe degradation (12,13). The concentration of water and alcohol and chain length of the alcohol greatly influence the reaction rate and degree of substitution (3,13).

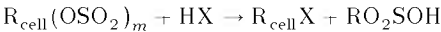
More highly substituted products have been obtained by reaction of cellulose with sulfuric acid and acetic anhydride, H₂SO₄–(CH₃CO)₂O, (DS up to 2.8) or esterification with chlorosulfuric acid in pyridine or formamide (14). Sulfation of cellulose utilizing the SO₃–DMF complex (15,16) to water-soluble, high viscosity CS is known. Homogeneous reaction systems include N₂O₄–DMF with SO₃–DMF, which proceed through a nitrite intermediate (17). Also used is N₂O₄–DMF with NOSO₄ in DMF (18). DS values of 0.3 to 2.0 and solution viscosities up to 7000 mPa·s(–cP) can be obtained by these processes (19).

The sodium salt of CS [9005-22-5] is prepared by reaction of cellulose with sulfuric acid in alcohol followed by sodium hydroxide neutralization (20). This water-soluble product yields relatively stable, clear, and highly viscous solutions. Introduced as a thickener for aqueous systems and an emulsion stabilizer, it is now of no economic significance.

Mixed esters such as cellulose acetate sulfate [51910-28-2] (21,22), cellulose acetate butyrate sulfate [57485-48-0] (21,22), cellulose acetate propionate sulfate [67351-39-7] (23), and ethylcellulose sulfate (24) are described in the patent literature but are not of commercial importance.

CS derivatives–salts have found limited use as detergents (25), antistatic coatings for photographic film (26), oil drilling fluids (25), thickeners in food, cosmetics, and pharmaceuticals (27). They have been recommended for use as cation exchangers (28,29). Also, sulfated polysaccharides have recently shown interesting antiviral activity (30).

CS esters react with hydrogen halides (28,29,31) to yield deoxy halogenated products.



Halogenation of sulfoxylated fibers yields materials with excellent flame-retardant properties (32).

Phosphorus-Containing Cellulose Esters. Cellulose phosphate [9015-14-9] esters (CP) are of interest because of their inherent flame resistance and ion-exchange capability.

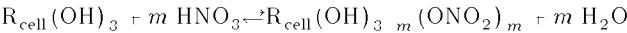
CP esters are generally prepared as the ammonium salt [9038-38-4] by the reaction of cellulose with phosphoric acid and urea at elevated temperatures (130–150°C). The effects of temperature and urea–H₃PO₄–cellulose composition on product analysis have been investigated (33). One of the first commercially feasible flameproofing procedures for cotton fabric, the Ban-Flame process (34,35), was based on this chemistry. It consists of mixing cellulose with a mixture of 50% urea, 18% H₃PO₄, and 32% water. It is then pressed to remove excess solution, heated to 150–175°C for 5–30 minutes, and thoroughly washed (36).

CP can also be prepared by the reaction of cellulose with phosphorus oxychloride in pyridine (37) or ether in the presence of sodium hydroxide (38). For the most part these methods yield insoluble, cross-linked, CP with a low DS. A newer method based on reaction of cellulose with molten urea–H₃PO₄ is claimed to give water soluble CP (39). The action of H₃PO₄ and P₂O₅ on cellulose in an alcohol diluent gives a stable, water-soluble CP with a high DS (>5% P) (40). These esters are flame resistant and have viscosities up to 6000 mPa·s(–cP) in 5 wt % solution. Cellulose dissolved in mixtures of DMF–N₂O₄ can be treated with PCl₃ to give cellulose phosphite [37264-91-8] (41) containing 11.5% P and only 0.8% Cl. Cellulose phosphinate [67357-37-5] and cellulose phosphonate [37264-91-8] have been prepared (42).

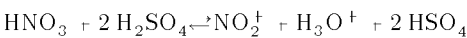
CP has been used as an ion-exchange material to remove radioisotopes, such as ⁹⁹Sr, ¹³⁷Cs (43) and U (VI) (44) from solution. CP ion-exchange resins have been used to remove calcium ions from blood (45) and calcium, magnesium, and potassium ions from wine (46). A commercial product made using CP, Calci-Bind, has been used for the treatment of kidney stones (47).

Cellulose Nitrate

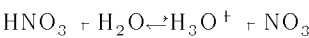
CN is the oldest and most important inorganic ester of cellulose. It is a white, odorless, and tasteless substance. It has found uses in plastics, lacquers, and explosives. CN is manufactured by treating cellulose with nitric acid in the presence of sulfuric acid and water. The amount of water determines the DS attained (11,48,49).



The nitration can be considered a typical esterification equilibrium. The removal of water with sulfuric acid forces the reaction to completion. It is believed the nitrating species is NO₂⁺, the nitronium ion (49,50).



The HNO₃–H₂SO₄ reaction competes with ordinary dissociation because of water.



Therefore, the amount of water present determines the concentration of NO₂⁺ and hence the extent of nitration. The degree of cellulose nitration is designated by the nitrogen content. The maximum commercial DS is ~2.9, which corresponds to 13.8% N. Products over 14% N have been obtained by special processes (51–54).

Manufacture.

Raw Material. Prior to World War II, CN was produced mainly from cotton linters because of their higher degree of purity (alpha cellulose >98%). The high purity linters allowed a higher yield and better quality product compared to those obtained from less pure wood pulps or other cellulose sources. The development of highly purified chemical-grade wood pulps has allowed this material to be used in the same manner as are linters.

The viscosity range of CN products can be adjusted in advance by choosing the starting cellulose with an appropriate degree of polymerization (DP). A study of the different celluloses examined the impact of various cellulose properties, such as morphological factors (percent crystallinity, fiber length, and distribution), chemical composition (DP, ash content), and hemicellulose and lignin content, on the nitration behaviors of cellulose (55).

Manufacturing Methods. Industrial-scale nitration is still frequently carried out using a batch process (Fig. 1). A rather small quantity of cellulose is agitated vigorously in a vessel containing a large excess (1:20 to 1:50) of HNO₃-H₂SO₄ nitrating mixture. The proper HNO₃:H₂SO₄ ratio (Table 1) is chosen to yield the desired degree of nitration and to help maintain fibrous structure by removing heat from the reaction. After 20–30 minutes of nitration, the mixture is centrifuged to remove excess acid, which is recycled. The CN is then immediately placed in a large excess of water to displace the adhering acid. The water slurry (~1% CN) is pumped to the purification area where it is centrifuged to remove spent acids for reconstitution and recycling. The yield of common CN (DS 1.8–2.7) is about 125 to 150^o %, with respect to starting cellulose. The losses arise from decomposition of cellulose and from mechanical losses in the ensuing separation steps.

Table 1. Variation of Ester Nitrogen Content with Water Content of Nitrating Bath^a

Composition of nitrating bath			Cellulose nitrate ester	
Water, %	Sulfuric acid, %	Nitric acid, %	Nitrogen content, %	DS
8.5	66.5	25	13.4	2.7
12.0	66.0	22	13.2	2.6
15.2	59.8	25	12.6	2.4
16.0	64.0	20	12.5	2.4
18.4	56.6	25	11.3	2.1
19.3	55.7	25	10.7	1.9
21.0	60	21	10.7	1.9

^a Ref. 48.

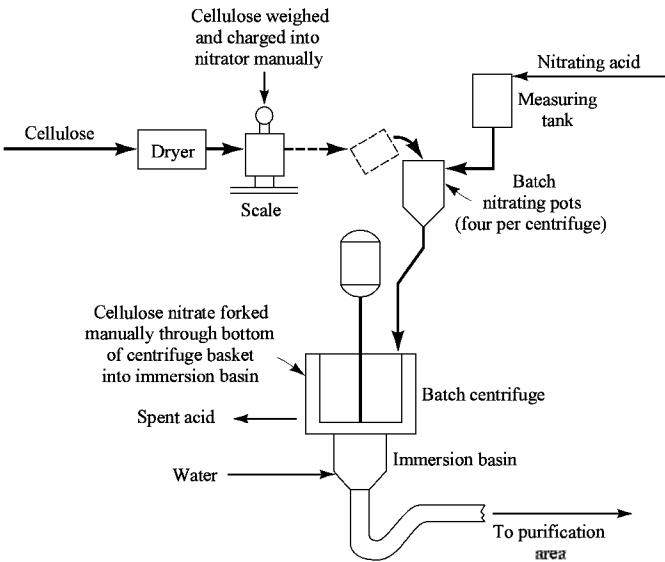


Fig. 1. Flow diagram of nitration by batch process.

Continuous nitration processes, which were developed in the 1960s, are more economical and provide a more uniform product (56) (Fig. 2). Cellulose and the nitrating acids are fed simultaneously into a vessel where nitration occurs. There it remains for 30–55 minutes. A newer process utilizing a continuous loop-formed pressure reactor (57) reduces the hold-up time to 6–12 minutes. The nitration mixture is continually withdrawn from the final zone of the reaction vessel and fed to a centrifuge. The centrifuge separates the spent acids and the CN is washed in stages with progressively weaker aqueous acids. Finally, the resulting water slurry of CN is pumped to the purification area. A pollution-free continuous process has been described (58). Cellulose strips have been continuously nitrated by drawing them through a bath of nitric acid, phosphoric acid, and water (59). A continuous flow apparatus for cellulose nitration has been described (60). A process using Mg(NO₃)₂ as the dehydrating agent, instead of H₂SO₄, has also been developed (61). This nitrating system is also appropriate for a continuous process.

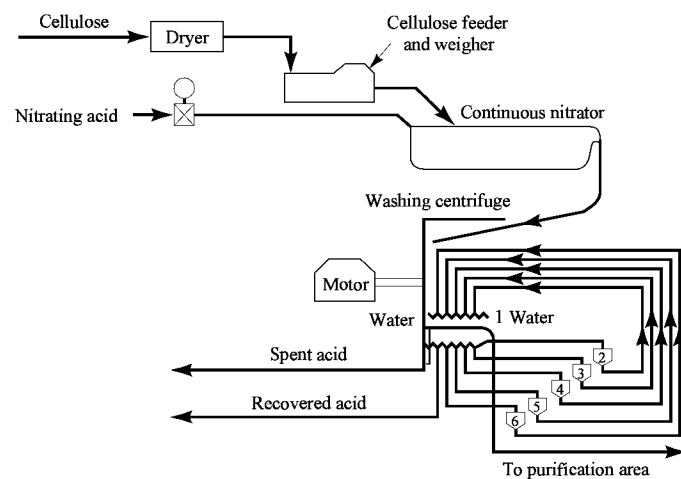


Fig. 2. Flow diagram of nitration of cellulose by Hercules continuous process.

Stabilization and Digestion. Following the initial washing steps, the stabilization of CN occurs. This involves removal of any remaining sulfuric acid since it would catalyze the decomposition of CN. The sulfuric acid present is both physically entrained in the product and chemically bonded to the cellulose chain. CN can contain 0.2–3% esterified H₂SO₄, depending on the DS of nitration. The sulfonate ester can be easily removed by saponification in boiling water with 0.5–1% acid residue. Boiling time can vary from 6–40 hours for batch processes. A continuous process has been developed (62).

CN is manufactured over a viscosity range of from 0.25 to 5000 mPa·s (cP) depending on end use (11). The final viscosity of the CN is adjusted in the digestion or pressure boiling step. A slurry of CN (6–8%) is heated, under pressure, to 130–150°C. This process can be achieved batchwise in autoclaves and continuously by pumping the slurry through long coils of piping (1200–1500 m) (14). During this step, viscosity can be reduced 10-fold in three hours at 132°C (Fig. 3). This viscosity reduction allows the production of CN suitable for higher solids and protective lacquers. Additional washing is necessary to remove any decomposition products generated during this step.

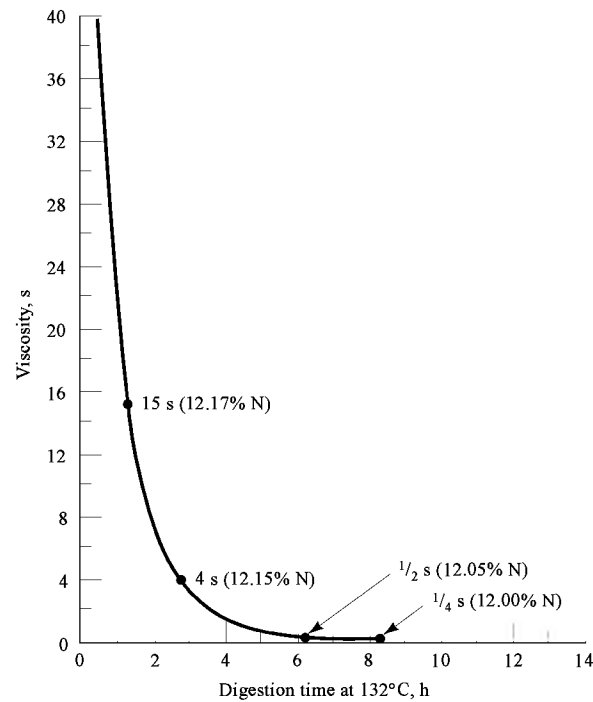


Fig. 3. Rate of viscosity reduction of cellulose nitrate on digestion in water at 132°C. The viscosities (falling-ball method) were determined in 12.2% solution.

Further stabilization against thermal and photochemical degradation may be necessary in some end uses. Certain organic acids such as citric, tartaric, stearic (63), and oxalic (64) have been used to stabilize CN against thermal degradation and discoloration during aging. Heat stabilization can be aided by incorporating diphenylamine [122-39-4] and epoxy compounds (65). It is believed these stabilizers act as acid scavengers. Discoloration by exposure to light can be reduced by addition of small amounts of dibenzoylmethane [120-46-7] (66).

Dehydration. Dry CN is extremely flammable; CN with high N content may explode when heated or subjected to sudden shock. Therefore, it is necessary to ship and handle CN wet with water or an alcohol. After the digestion process and centrifugation, a wet CN containing 25–35% water remains. This may be packed as is and shipped. More frequently, the water is displaced with an alcohol, typically ethanol or 2-propanol, by displacement presses or displacement centrifuges. Continuous processes prevail here also (67). The alcohol-wet CN is pressed to 30–35 wt % alcohol and shredded before packaging and shipping. Alcohol-wet CN fibers are more readily soluble in organic lacquer solvents than dry CN (11).

The water-wet CN can be gelatinized with softeners such as phthalates and dried on drums or band driers for the manufacture of CN chips (68). These CN chips can be colored with pigments so that colored enamels can be produced without using ball or roller mills.

Alternative Nitrating Systems. Many nitrating systems have been investigated with the objective of finding an improved method or an increase in the DS (69–71). Some of these methods are able to produce high molecular weight CN with a high DS (polymer analogous nitration). Some of these procedures are shown in Table 2. However, none of these systems has replaced the HNO₃–H₂SO₄–H₂O ternary system for industrial usage.

Table 2. Alternative Cellulose Nitrating Systems

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Nitrating system	N max, %	Remarks
HNO ₃		
<75%		unstable Knecht compound formed
78–85°	8	CN dissolves in acid solution
85–89°	10	
90–100°	13.3	
HNO ₃ and inorganic salts	13.9	sulfates, nitrates, phosphates
HNO ₃ and CH ₂ Cl ₂	14.0	polymer analogous
HNO ₃ CH ₃ COOH (CH ₃ CO ₂)O	14.1	polymer analogous
HNO ₃ H ₃ PO ₄ P ₂ O ₅	14.0	polymer analogous

Nitrating cellulose with pure HNO₃ is the simplest method of obtaining CN. In practice, nitration does not occur with acid concentrations below ~75%. At acid concentrations <75%, an unstable compound (so called Knecht compound) is formed which has been described as a molecular complex or an oxonium salt of the nitric acid (72). HNO₃ concentrations of 75–85° yield CN with 5–8° N, which dissolve in excess acid. CN with ° N of 8–10° are formed at acid concentrations of 85–89°. Above 89°, a heterogeneous nitration occurs without apparent swelling of the cellulose fibers. CN with 13.3° N can be obtained with 100° HNO₃. Addition of inorganic salts to 100° HNO₃ can raise the ° N to 13.9.

There are a variety of reaction systems that allow the formation of cellulose trinitrate [9046-47-3]. HNO₃ in methylene chloride, CH₂Cl₂, yields a trinitrate with essentially no degradation of the cellulose chain (53). The HNO₃ acetic acid acetic anhydride system is also used to obtain the trinitrate product with the fiber structure largely intact (51,52). Another polymer analogous reaction utilizes a 1:1 mixture of HNO₃ and H₃PO₄ with 2.5° P₂O₅ to achieve an almost completely nitrated product (54).

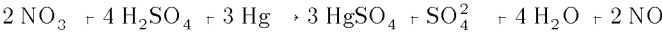
Analysis. Specifications and tests for soluble CN have been adopted by ASTM and are described (48,73–75). Brief descriptions of the most important tests are given here.

Drying. Flammability increases dramatically when drying CN, and thus great care should be taken when drying CN for analysis. Small quantities may be dried by spreading the water or alcohol-wet sample in a thin layer and air drying for 12–16 hours followed by oven drying at 100–105°C for one hour. Larger samples should be dried by passing a stream of warm (60–65°C) air through the sample.

Stability. Heat stability is determined by measuring the time required for a specific amount of CN, held at 134.5°C, to decompose and discolor methyl violet test paper (75).

Solution Viscosity. Solution viscosity is determined in solvent blends of toluene, ethyl alcohol, and ethyl acetate. The solvent blend and concentration of CN varies according to the viscosity and nitrogen content of the CN being tested. Viscosities are measured at 25°C by the falling-ball method. The results are ordinarily expressed in terms of seconds required for a 2.4 mm diameter steel ball to fall a distance of 5.08 cm through the designated solvent (ASTM method D1343).

DS or N Content. The traditional method to determine the ° N content of a particular CN relies on the decomposition of CN with H₂SO₄ over mercury.



The liberated NO gas is collected in a nitrometer and converted to ° N (48,74).

Another method used to determine the DS of CN, and other inorganic esters, is nuclear magnetic resonance (nmr). Both solution ¹H and ¹³C (76) and solid-state ¹³C nmr (77) have been found to be very useful for qualitative and quantitative determination of DS of CN. One drawback to studying CN in solution is that no one solvent or solvent system can be utilized for the complete DS range. Typical solvents used have been acetone and DMSO; however, these solvents do not dissolve CN with DS < 1.8. Another complication that affects solubility at higher DS is heterogeneous nitration, which is dependent on the nitration method used (78). The resulting measurement problems can be overcome by using solid-state ¹³C nmr (79), albeit with some loss in resolution. Again, sample preparation may lead to differences in spectral analysis because of nitration heterogeneity. Nmr has also been used to study CS (80,81).

Methylation of free OH groups, followed by denitration, hydrolysis, reduction, and glc analysis has been suggested as a method for determining the location of nitrate (82). This method has been suggested for CP and CS (82) as the phosphate and sulfate groups are stable to methylation and can then be removed. Periodate oxidation has been used to determine the DS of CS (81).

Uses. Cellulose nitrates with differing nitrogen contents have various applications (Table 3). The largest industrial use of CN is protective and decorative lacquer coatings. CN is soluble in a variety of organic solvents and yields clear, tough films. CN is also compatible with many plasticizers and resins.

Table 3. Applications of CNs of Varying Nitrogen Content and DS

CN type	N, %	DS
celluloid	10.5–11.0	1.8–2.0
alcohol-soluble CN	10.9–11.3	1.9–2.1
ester-soluble CN	11.8–12.2	2.2–2.3
gun cotton	13.0–13.6	2.6–2.8

In addition, CN lacquers are easy to apply by spraying (air-less, compressed air, and electrostatic), have excellent adhesion, solvent release properties, and pigment dispersability. The disadvantages of CN include flammability, yellowing, and low solids content at sprayable viscosities (20–25°). CN lacquers are used in coatings for wood furniture and fixtures. Additional markets include coatings for leather, OEM automobile finishes and refinishes, rotogravure and flexographic inks, and other coatings applications.

The largest market for CN-based lacquers is for auto and wood furniture coatings (qv). The U.S. consumption of CN for these two markets is estimated at 15,500 t for 1991. Because of low solids content of typical CN-based lacquers, much work is being done to lower the volatile organic content (VOC) of CN lacquers. Areas of investigation include higher solids levels and uv curable coatings. Waterborne CN systems (83) have generated considerable interest because of their much lower VOC. However, problems with grain raising and clarity have been encountered with water-based wood coatings.

CN coatings are used in leather coatings because of highly desirable clarity, liveliness, gloss, and sealing. However, the leather coatings industry is under pressure to reduce VOC in order to protect the environment. As a result, increasing quantities of water-based and intermediate solids coatings are being investigated and used. One small but relatively steady market for CN is fingernail polish. CN is the base resin for almost all nail polishes. Approximately 341 t yr of CN are used in these products.

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CELLULOSE ETHERS

General Considerations

Alkylation of cellulose yields a class of polymers generally termed cellulose ethers. Most of the commercially important ethers are water-soluble and are key adjuvants in many water-based formulations. The most important property these polymers provide to formulations is rheology control, ie, thickening and modulation of flow behavior. Other useful properties include water-binding (absorbency, retention), colloid and suspension stabilization, film formation, lubrication, and gelation. As a result of these properties, cellulose ethers have permeated a broad range of industries including foods, coatings, oil recovery, cosmetics, personal care products, pharmaceuticals, adhesives, printing, ceramics, textiles, building materials, paper, and agriculture.

Estimates from SRI International figures indicate that the world consumption, excluding eastern European countries and the former Soviet Union, of all grades of cellulose ethers in 1987 was about 230,000 t (1). Cellulose ethers represent a mature industry with annual sales of over one billion dollars and annual growth rate averaging 2–3% per year. The U.S. consumption in 1987 was approximately 69,000 t, Western Europe about 116,000 t, and Japan about 22,000 t. Prices for the principal products range from about \$1.65/kg for crude grades of sodium carboxymethylcellulose to over \$11/kg for purified hydroxypropylcellulose. The highest volume cellulose ethers, the industry workhorses, are sodium carboxymethylcellulose, hydroxyethylcellulose, and hydroxypropylmethylcellulose. Cellulose ethers as a class compete with a host of other materials including natural gums, starches, proteins (qv), synthetic polymers, and even inorganic clays (see CARBOHYDRATES; GUMS). They provide effective performance at reasonable cost and are derived from a renewable, natural resource.

Cellulose ethers are manufactured by reaction of purified cellulose with alkylating reagents under heterogeneous conditions, usually in the presence of a base, typically sodium hydroxide, and an inert diluent. Cottonseed linter fiber and wood fiber are the principal sources for cellulose. Purified cellulose cotton linters, commonly termed chemical cottons, are generally of higher purity and higher maximum molecular weight than purified cellulose from dissolving grades of wood pulp. The base, in combination with water, activates the cellulose matrix by disrupting hydrogen-bonded crystalline domains, thereby increasing accessibility to the alkylating reagent. This activated matrix is commonly termed alkali cellulose (2–6). The base also promotes the etherification reaction. The several purposes of the inert diluent are to suspend/disperse the cellulose, provide heat transfer, moderate reaction kinetics, and facilitate recovery of the product. Crude grades of cellulose ethers, most notably sodium carboxymethylcellulose, may be made in the absence of any diluent. Reactions are typically conducted at elevated temperature, ~50 to 140°C, and under nitrogen to inhibit oxidative molecular weight degradation of the polymer (7,8), if so desired. After reaction, crude grades are simply dried, ground, and packed out; purified grades require removal of byproducts in a separate operation prior to drying. Various additives, such as colloidal silicas, may be added in small amounts to some products prior to drying or before packout to improve dry handling properties. In addition to these unit operations, schematically outlined in Figure 1, a molecular weight reduction operation may be included in the process at any of several points, most notably either in the reaction vessel (before, during, or after the alkylation reaction), after purification before drying, or treatment of dry material (9–11). Hydrogen peroxide is commonly used, though deliberate degradation may also be induced through controlled alkaline-catalyzed autoxidation with oxygen (air) in the reactor. Acids can also be used to cleave the cellulose chain (12,13).

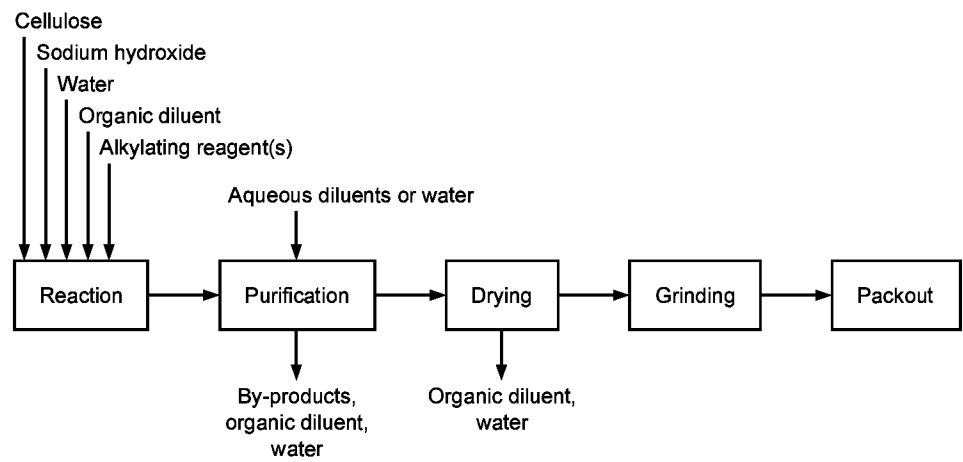
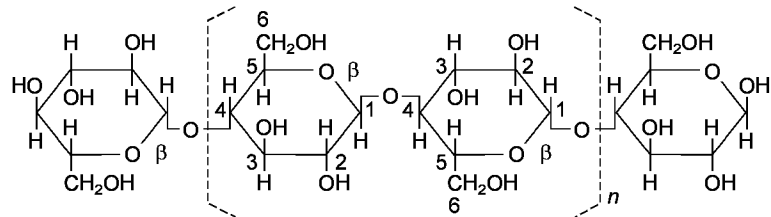


Fig. 1. Unit operations for the manufacture of purified cellulose ethers.

An important characterization parameter for cellulose ethers, in addition to the chemical nature of the substituent, is the extent of substitution. As the Haworth representation of the cellulose polymer shows, it is a linear, unbranched polysaccharide composed of glucopyranose (anhydroglucose) monosaccharide units linked through their 1,4 positions by the β anomeric configuration.



The structurally similar starch amylose polymer is linked through the α anomeric configuration. The three hydroxyl functions per anhydroglucose unit are noteworthy; these hydroxyls are the active sites for ether formation.

The extent of substitution is described as the degree of substitution (DS), defined as the average number of hydroxyl groups substituted per anhydroglucose unit. Excluding the terminal residues, each anhydroglucose moiety has three available hydroxyl groups for a maximum DS value of three. In certain cases the alkylating reagent, such as an alkylene oxide, generates a new hydroxyl group upon reacting which can then further react to give

oligomeric chains. The product is then characterized by its molar substitution (MS), the moles of reagent combined per mole of anhydroglucose unit. The ratio of MS to DS is a measure of the average chain length of the oligomeric side chains. Organo-soluble ethylcellulose has a DS of 2.3–2.8. Most water-soluble derivatives have DS values of 0.4–2.0. Hydroxyalkyl ethers have MS values typically between 1.5 and 4.0.

MS and DS values are average values, placing no significance on the formal distribution of the substituents within or among polymer chains. Substituent distribution, however, is an important molecular parameter affecting solution rheology and ultimately end use properties. A classic example is offered by sodium carboxymethylcellulose (14). Depending on reaction conditions, sodium carboxymethylcellulose (CMC) of DS ~0.80 can be made to exhibit a varying degree of solution thixotropy, the effect being dependent not so much on degree of substitution but rather on the distribution of substituents.

Thixotropic solutions are characterized by a decrease in viscosity on shearing followed by a time-dependent increase after the shear stress is removed. A plot of shear rate versus shear stress reveals a hysteresis loop. Association among polymer chains via electrostatic, hydrogen-bonding, or hydrophobic effects can lead to thixotropy. Carboxymethyl substituent uniformity along the polymer chain affects thixotropic behavior of CMC because regions of contiguous unsubstituted anhydroglucose units, ie, blocks, among polymer chains tend to associate through hydrogen bonding (15). The extent of blockiness is controlled by reaction conditions. Solution thixotropy is important in applications requiring suspension or stabilization of particulates.

As substituent uniformity is increased, either by choosing appropriate reaction conditions or by reaction to high degrees of substitution, thixotropic behavior decreases. CMCs of DS > 1.0 generally exhibit pseudoplastic rather than thixotropic rheology. Pseudoplastic solutions also decrease in viscosity under shear but recover instantaneously after the shear stress is removed. A plot of shear rate versus shear stress does not show a hysteresis loop.

Other examples illustrating the effect of substituent distribution on properties include: (1) enzymatic stability of hydroxyethylcellulose (16,17); (2) salt compatibility of carboxymethylcellulose (18,19); and (3) thermal gelation properties of methylcellulose (20). The enzymatic stability of hydroxyethylcellulose is an example where the actual position of the substituents within the anhydroglucose units is considered important. Increasing substitution at the C2 position promotes better resistance toward enzymatic cleavage of the polymer chain. Positional distribution is also a factor in the other two examples.

¹³C-nmr is the premier method for the compositional and structural characterization of cellulose ethers (21–27). Another analytical method is based on chromatography of hydrolyzates (28). The results show that the reactivity of the three hydroxyl groups can vary significantly depending on the alkylating reagent, the type of reaction, and reaction conditions. For most cellulose ethers, substitution occurs primarily at the C2 and C6 hydroxyl groups (29).

Aside from the chemical nature of the substituent and its DS (MS) and distribution, solution viscosity, ie, polymer molecular weight, is another important characterization parameter. Generally, manufacturers supply cellulose ethers in different viscosity grades, made by choosing a cellulose furnish of appropriate molecular weight or by reducing the molecular weight during processing (9–11). Most manufacturers specify solution viscosity data and not polymer molecular weight in their technical literature; however, molecular weight can be estimated from the classical Mark-Houwink equation:

$$[\eta] = K M^a$$

where [η] is intrinsic viscosity, *K* and *a* are empirically derived constants, and *M* is the viscosity-average molecular weight, which approximates the weight-average molecular weight. Values of *K* and *a* for various cellulose ethers are available (30–32).

Molecular weight from solution viscosity measurements represents an average value of polymer chain lengths. The distribution of chain lengths making up a polymer fraction is commonly termed molecular weight distribution (MWD), a parameter that can influence performance properties, particularly mechanical properties of films. Size exclusion chromatography (sec), also termed gel-permeation chromatography (gpc), has been the classical method for determining MWD. However, the lack of suitable columns hindered development of aqueous sec methods for water-soluble polymers until the 1980s. Now, because of the development of high performance packings and columns, the MWD of water-soluble cellulose ethers is a measurable parameter (33–36).

Many cellulose ethers contain mixed substituents (cellulose mixed ethers) in order to enhance or modify the properties of the monosubstituted derivative. For example, incorporation of low levels of hydroxypropyl or hydroxyethyl groups into methylcellulose increases its thermal gelation and flocculation temperatures in aqueous media. Carboxymethylation of hydroxyethylcellulose produces a product having excellent tolerance to mono- and divalent metal ions in solution but which readily cross-links with tri- or tetravalent ions to give highly viscoelastic gels. The solubility of ethylcellulose in organic aliphatic solvents is improved by incorporating hydroxyethyl moieties. A fairly new commercial cellulose ether composition is a mixed ether, hydroxyethylcellulose modified with hydrophobic long-chain hydrocarbyl groups (37–39). The hydrophobic groups promote polymer chain association in solution, drastically altering rheology and surface activity properties.

Health and Safety Factors. No adverse toxicological or environmental factors are reported for cellulose ethers in general (14,39–50). Some are even approved as direct food additives, including purified carboxymethylcellulose, methylcellulose, hydroxypropylmethylcellulose, and hydroxypropylcellulose.

The only known hazard associated with cellulose ethers is that they may form flammable dusts when finely divided and suspended in air, a hazard associated with most organic substances. An explosion may result if suspended dust contacts an ignition source. Cloud and layer ignition temperatures generally vary between 290 and 410°C (51). Critical air-borne concentrations vary depending on particle size. This hazard can be minimized largely through good housekeeping and proper design and operation of handling equipment.

Another minor hazard is that water-soluble cellulose ether powders form a slippery surface when wet; therefore, spills should be cleaned promptly to avoid slipping accidents.

Commercial Cellulose Ethers

SODIUM CARBOXYMETHYLCELLULOSE

Properties. Sodium carboxymethylcellulose [9004-32-4] (CMC), also known as cellulose gum, is an anionic, water-soluble cellulose ether, available in a wide range of substitution. The most widely used types are in the 0.7 to 1.2 DS range. Water solubility is achieved as the DS approaches 0.6; as the DS increases, solubility increases. The rate at which CMC dissolves depends primarily on its particle size. Finely ground material dissolves faster than coarser grades. The coarse material, however, does not agglomerate as readily when added to water and is therefore easier to disperse. The rate of dissolution also increases with increasing substitution and decreasing molecular weight, ie, viscosity. High molecular-weight grades of CMC have viscosities as high as 12,000 mPa·s(=cP) at 1° solids (as recorded on a Brookfield LVT Viscometer at 30 rpm). Lower molecular-weight CMCs have viscosities in water as low as 50 mPa·s(=cP) at 4° solids.

CMC is soluble in hot and cold water. Solutions may be pseudoplastic or thixotropic depending on molecular weight, DS, and manufacturing process. High molecular-weight, low DS CMCs tend to be more thixotropic. Solutions are viscosity stable at ambient temperature over a wide range of pH. In general, maximum solution viscosity and best stability are obtained at pH 7 to 9. Above pH 10, a slight viscosity decrease is observed. As pH is lowered below 4, viscosity may first increase then decrease as intermolecular associations among free acid groups start affecting solubility. CMC is not soluble in organic solvents, but dissolves in mixtures of water and water-miscible solvents such as ethanol or acetone. Low viscosity CMCs are more tolerant of higher levels of organic solvents.

Monovalent cations are compatible with CMC and have little effect on solution properties when added in moderate amounts. An exception is silver ion, which precipitates CMC. Divalent cations show borderline behavior and trivalent cations form insoluble salts or gels. The effects vary with the specific cation and counterion, pH, DS, and manner in which the CMC and salt are brought into contact. High DS (0.9–1.2) CMCs are more tolerant of monovalent salts than lower DS types, and CMC in solution tolerates higher quantities of added salt than dry CMC added to a brine solution.

CMC is compatible with most water-soluble nonionic gums over a wide range of concentrations. When a solution of CMC is blended with a solution of a nonionic polymer such as hydroxyethylcellulose or hydroxypropylcellulose, a synergistic effect on viscosity is usually observed. Such blends

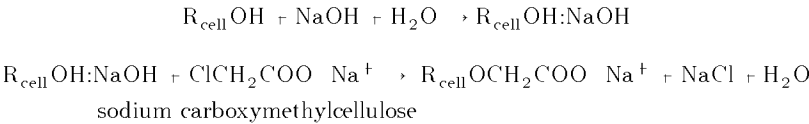
produce solution viscosities considerably higher than would ordinarily be expected. This effect is reduced if other electrolytes are present in the system. Some typical properties of commercial CMCs are given in Table 1.

Table 1. Typical Properties of Purified CMC^a

Property	Value	
	Powder	
appearance	white to off-white	
assay, dry basis, min %	99.5	
moisture, max %	8.0	
browning temp, °C	227	
charring temp, °C	252	
bulk density, g cm ³	0.75	
molecular weight, M_w	9.0×10^4	7.0×10^5
	Solution	
viscosity, Brookfield, 30 rpm, mPa·s(cP)		
at 1% solids (high M_w)	~6000	
at 4% solids (low M_w)	~50	
sp gr, 2% at 25°C	1.0068	
pH, 2%	7.5	
surface tension, 1%, mN m(dyn cm)	71	
refractive index, 2% at 25°C	1.3355	
	Film	
refractive index	1.515	

^a Ref. 14.

Manufacture. Common to all manufacturing processes for CMC is the reaction of sodium chloroacetate [3926-62-3] with alkali cellulose complex represented here as R_{cell}OH:NaOH:



A by-product is sodium glycolate [2836-32-0] (sodium hydroxyacetate):



Generally, monochloroacetic acid [79-11-8] (MCA) is added to the reaction slurry containing sufficient excess sodium hydroxide to neutralize the MCA and effect its reaction. The use of esters of MCA has also been reported (52). Common reaction diluents are isopropyl alcohol, *t*-butyl alcohol, or ethyl alcohol (53,54). Dimethoxyethane has also been reported to be effective (55). The product is isolated and washed with aqueous alcohol or acetone to remove by-product salts. Unpurified crude grades are generally prepared in the absence of diluents (56–59).

Economic Aspects. CMC is the most widely used cellulose ether. Excluding the former Soviet Union and Eastern Bloc countries, from which little data are available, world consumption of crude and purified grades totaled approximately 123,000 metric tons in 1987 (Table 2). Annual growth rate is nominal at 1–2%. The total volume in the United States declined in the 1980s from ~32,000 metric tons in 1981 to ~19,500 in 1987 because of decreased oil well drilling activity, an important outlet.

Table 2. World Supply and Demand for CMC^a, 10³t

Region	Capacity ^b	Production	Consumption	Imports	Exports
United States	26	19.5	27.5	10.0	4.0
Western Europe	184	99	66	1	33
Japan	44	25	16	<1	9
Canada, Latin America, other Asia			13		
<i>Total</i>	<i>254</i>	<i>143.5</i>	<i>122.5</i>		

^a In 1987 (1).

^b Crude and purified grades, expressed in 100% CMC.

In the United States Aqualon Co., a Hercules Incorporated Company, is the largest producer, followed by Carbose Corp. and MAK Chemical Corp. Western Europe has about 14 companies manufacturing CMC; the five largest are Metsa Serla in Finland, Aqualon France SA in France, Hoechst AG in Germany, Billerud AB in Sweden, and AKZO in The Netherlands and Italy. Among the six producers in Japan, Dai-ichi Kogyo Seiyaku (DKS) and Diacel Chemical Industries are the two largest.

Specifications and Standards; Test Methods. Certain types of purified sodium carboxymethylcellulose meet standards set by the *U.S. Code of Federal Regulations* (CFR) Title 21, Section 182.1745, substances that are generally recognized as safe (GRAS). The FDA defines the direct food additive as the sodium salt of carboxymethylcellulose, not less than 99.5% on a dry weight basis, with a maximum substitution of 0.95 carboxymethyl groups per anhydroglucose unit, and with a minimum viscosity of 25 mPa·s(cP) in a 2% (by weight) aqueous solution at 25°C.

Cellulose gum is the accepted common name for purified CMC. It may be used in milk products, dressings, jellies, syrups, beverages, and other select products. It is permitted in food contact and packaging applications.

Sodium carboxymethylcellulose is listed in the 1990 *United States Pharmacopeia* under the categories of pharmaceutical aid (suspending agent, tablet binder, viscosity-increasing agent), and cathartic tablets.

Procedures for the analysis of CMC are available in manufacturers' bulletins (14).

Uses. CMC is an extremely versatile polymer, and it has a variety of applications. A sampling of significant applications is given in Table 3. A more extensive listing can be found in reference 14.

Table 3. Applications for CMC^a

Industry	Application	Function
foods	frozen desserts	inhibit ice crystal growth
	dessert toppings	thickener
	beverages, syrups	thickener, mouthfeel
	baked goods	water-binder, batter viscosifier
	pet food	water-binder, thickener, extrusion aid
pharmaceuticals	tablets	binder, granulation aid
	bulk laxatives	water-binder
	ointments, lotions	stabilizer, thickener, film-former
cosmetics	toothpaste	thickener, suspension aid
	denture adhesives	adhesion promoter
	gelled products	gellant, film-former
paper products	internal additive	binder, improve dry-strength
	coatings, sizes	water-binder, thickener
adhesives	wallpaper paste	adhesion promoter, water-binder
	corrugating	thickener, water-binder, suspension aid
	tobacco	binder, film-former
lithography	fountain, gumming	hydrophilic protective film
ceramics	glazes, slips	binder (promotes green strength)
	welding rods	binder, thickener, lubricant
detergents	laundry	soil antiredeposition aid
textiles	warp sizing	film-former, adhesion promoter
	printing paste, dye	thickener, water-binder

^a Ref. 14.

HYDROXYETHYLCELLULOSE

Properties. Hydroxyethylcellulose [9004-62-0] (HEC), is a nonionic polymer. Low hydroxyethyl substitutions (MS = 0.05–0.5) yield products that are soluble only in aqueous alkali. Higher substitutions (MS > 1.5) produce water-soluble HEC. The bulk of commercial HEC falls into the latter category. Water-soluble HEC is widely used because of its broad compatibility with cations and the lack of a solution gel or precipitation point in water up to the boiling point. The MS of commercial HEC varies from about 1.8 to 3.5. The products are soluble in hot and cold water but insoluble in hydrocarbon solvents. HEC swells or becomes partly to mostly soluble in select polar solvents, usually those that are miscible with water.

Commercially, HEC is available in a wide range of viscosity grades, ranging from greater than 500 mPa·s(cP) at 1% solids to less than 100 mPa·s(cP) at 5% total solids. Because HEC is nonionic, it can be dissolved in many salt solutions that do not dissolve other water-soluble polymers. It is soluble in most 10% salt solutions and in many 50% (or saturated) salt solutions such as sodium chloride and aluminum nitrate. As a rule, the lower substitution grades are more salt-tolerant.

HEC is soluble in both hot and cold water; however, as with most water-soluble thickeners, the particles have a tendency to agglomerate, or lump, when first wetted with water. This is especially evident when the HEC is added to water with poor agitation. Manufacturers have eliminated the problem of lumping and slow dissolving by surface treating the particles, most commonly with glyoxal [107-22-2] (59–62). When added to water, the particles completely disperse. After an initial induction period, commonly termed the delayed hydration time, the dispersed particles begin to dissolve producing smooth, lump-free solutions. The delayed hydration time can be increased or decreased by lowering or raising, respectively, the pH. Most manufacturers supply dispersible grades.

Solutions of HEC are pseudoplastic. Newtonian rheology is approached by very dilute solutions as well as by lower molecular-weight products. Viscosities change little between pH 2 and 12, but are affected by acid hydrolysis or alkaline oxidation under pH and temperature extremes. Viscosities of HEC solutions change reversibly with temperature, increasing when cooled and decreasing when warmed.

HEC is generally compatible with other cellulosic water-soluble polymers to give clear, homogeneous solutions. When mixed with an anionic polymer such as CMC, however, interactions between the two polymers may result in synergistic behavior, ie, viscosities higher than predicted and calculated. HEC has excellent compatibility with natural gums.

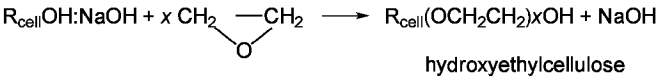
Some typical properties of HEC are given in Table 4.

Table 4. Typical Properties of HEC^a

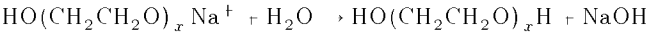
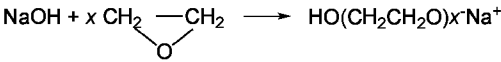
Property	Value
<i>Powder</i>	
appearance	white to light tan
moisture, max %	5.0
ash content (as Na ₂ SO ₄), %	5.5
bulk density, g cm ³	0.6–0.75
browning temp, °C	205–210
molecular weight, <i>M_w</i>	9 × 10 ⁴ –1.3 × 10 ⁶
<i>Solution</i>	
viscosity, Brookfield, 30 rpm, mPa·s(cP)	
at 1% solids (high <i>M_w</i>)	5000
at 5% solids (low <i>M_w</i>)	75
sp gr, 20%, g cm ³	1.0033
pH	7
surface tension, mN m(dyn cm)	
MS 2.5 at 0.1%	66.8
at 0.001%	67.3
refractive index, 20%	1.336
<i>File</i>	
refractive index	1.51
moisture content, %, at 25°C	
50% rh	6
84% rh	29

^a Ref. 40.

Manufacture. Purified hydroxyethylcellulose is manufactured in diluent-mediated processes similar to those used to produce carboxymethylcellulose except ethylene oxide [75-21-8] is used in place of MCA (63,64):



A competing reaction that consumes ethylene oxide is hydrolysis to ethylene glycol and oligomeric glycol by-products.



Because of the low boiling point of ethylene oxide, reactions are generally conducted in stirred autoclaves at elevated pressures.

Economic Aspects. A breakdown of salient 1987 world supply and demand figures for HEC is given in Table 5.

Table 5. World Supply and Demand For HEC^a, 10³ t

Region	Capacity	Production	Consumption	Imports	Exports
United States ^b	32	20.5	20.5	1.0	3.5
Western Europe	23	17	13		
Japan	1	1	1		
Canada, Latin America, other			4		
Asia					
Total	56	38.5	38.5		

^a In 1987 (1).

^b Includes carboxymethylhydroxyethylcellulose, which accounts for <5%.

Aqualon Co. and Union Carbide Corp. have manufacturing facilities in the United States and Western Europe. Hoechst AG in Europe and Fuji Chemical Co., Ltd. in Japan are the only other procedures of HEC.

Specifications and Standards; Test Methods. Hydroxyethylcellulose is included in the list of materials that are in compliance with requirements of the U.S. FDA for use in adhesives and in resinous and polymeric coatings employed on the food-contact surfaces of metal, paper, or paperboard articles, and other substrates intended for use in food packaging as specified in CFR 21. HEC made dispersible by cross-linking with glyoxal is cleared only as an adhesive and as a component of paper and paperboard in contact with food. It has not been cleared as a direct food additive.

Procedures for determining ash, moisture, solution preparation, and viscosity measurements can be found in manufacturers' product bulletins (40,41) and in ASTM D2364-69 (65).

Uses. HEC is used as a thickener, protective colloid, binder, stabilizer, and suspending agent in a variety of industrial applications. A guide to the principal uses is given in Table 6.

Table 6. Applications for HEC^a

Industry	Application	Function
coatings	latex paints	thickener
	polymer emulsions	protective colloid
construction	cements, mortars	thickener, water-binder, retarder
paper	coatings, sizes	thickener, water-binder
pharmaceuticals	lotions, ointments	thickener, stabilizer, water-binder
cosmetics	toothpastes	thickener
	shampoos	thickener
	creams, lotions	thickener, stabilizer
ceramics	welding rods	water-binder, extrusion aid
	glazes	water-binder (promotes green strength)

^a Ref. 40.

Mixed Ether Derivatives of HEC. Several chemical modifications of HEC are commercially available. The secondary substituent is generally of low DS (or MS), and its function is to impart a desirable property lacking in HEC.

Carboxymethylhydroxyethylcellulose (CMHEC). This is an anionic modification of HEC manufactured by Aqualon Co. Sodium carboxymethylhydroxyethyl-cellulose [9088-04-4] is manufactured by reaction of alkali cellulose either simultaneously or sequentially with ethylene oxide and sodium chloroacetate. Various grades, with carboxymethyl DS, CM(DS), of 0.3 to 0.5 and hydroxyethyl MS, HE(MS), of 0.7 to 2.0 are available. CMHEC has properties of both HEC and CMC. It is more compatible than CMC with salts because of the presence of nonionic hydroxyethyl groups. In saturated NaCl, only CMC with a CM(DS) > 1.0 is completely soluble. CMHEC, on the other hand, is soluble with a CM(DS) as low as 0.3. CMHEC is also very tolerant of Ca²⁺ and consequently readily dissolves in seawater. Unlike HEC, CMHEC in solution may be cross-linked with trivalent cations such as Fe³⁺ and Al³⁺ to give greatly increased viscosity or three-dimensional viscoelastic gels (66).

CMHEC products are used predominantly in oil recovery applications. The high water binding capability, salt compatibility, and adsorption to clay and mineral surfaces give CMHEC ethers excellent control over high salinity fluids (67,68). Water loss in cement slurries is also reduced (69). CMHEC is also used in hydraulic fracturing fluids. Gels formed by cross-linking with multivalent cations can suspend and transport proppants into a well bore and then fracture (66,70). Some typical properties of CMHEC having a CM(DS) ~0.3 and HE(MS) ~0.7 are listed in Table 7.

Table 7. Typical Properties of Mixed Ether Derivatives of HEC^a

Property	CMHEC	Cationic HEC	EHEC	HMHEC
	Powder			
appearance	off-white	light yellow	off-white	off-white
bulk density, g cm ³	0.6	0.48	0.4–0.8	0.55–0.75

ash content (as Na ₂ SO ₄), ° o		3	3 (as NaCl)	10 max
volatiles, ° o	6–8	7	8 max	5 max
	<i>Solution</i>			
pH	6.5–10	7	6–7 ~65	6–8.5
flocculation temp in water, °C				
surface tension, mN m(dyn cm)			55	~62
	<i>Film</i>			
tensile strength, MPa ^b	69 ^c	14–22 ^c	45–55 ^d	
flexibility ^e		60–70 ^c	25–35 ^d	
refractive index	1.530		1.49	

^a Refs. 39, 47, 49, 71.
^b To convert MPa to psi, multiply by 145.
^c At 50° o rh.
^d At 65° o rh.
^e MIT double folds.

Cationic Hydroxyethylcelluloses. These materials are manufactured by Union Carbide Corp. and National Starch and Chemical Corp., marketed under the trade names Polymer JR and Celquat, respectively (47,48). The cationic substituent on Polymer JR is presumably 2-hydroxypropyltrimethylammonium chloride (72). Celquat is presumably the reaction product of HEC with *N,N*-diallyl-*N,N*-dimethylammonium chloride (73). Their primary application is in shampoos and hair conditioners wherein the cationic moiety imparts substantivity to hair. Some typical properties of Celquat resins are given in Table 7.

Hydrophobic Hydroxyethylcelluloses. These materials are produced by stepwise or simultaneous reaction of ethylene oxide and a hydrophobic alkylating reagent. Commercial products include: ethylhydroxyethylcellulose [9004-58-9] (EHEC), manufactured by Berol Kemi AB under the Bermocoll trade name (49), and HEC modified with a long-chain alkyl group, generically termed HMHEC (where HM = Hydrophobically Modified), manufactured by Aqualon Co. and sold under the trade name Natrosol Plus (39). These products are water-soluble. An organo-soluble ethyl modification is also available, which is classified as a derivative of ethylcellulose.

Water-soluble EHEC is a moderate ethyl DS (~1.0) modification of high hydroxyethyl MS (<2.0) HEC. Ethyl groups lower the surface and interfacial tensions, thereby increasing surface activity. This group also modifies adsorption properties of the polymer to particulates found in many formulations such as clays, pigments, and latices. Aqueous solutions have pseudoplastic rheology. High viscosity grades are more pseudoplastic than low viscosity materials, which approach Newtonian flow behavior. Viscosities decrease reversibly with increasing temperature. Above 65°C, EHEC precipitates from solution. Salts lower the temperature at which precipitation occurs. Solution viscosities are insensitive to pH between about 3 to 11. Aqueous solutions are miscible with lower alcohols, glycols, and ketones up to equal proportions. Water-soluble EHECs are used to thicken and stabilize a variety of materials, including water-borne paints, plasters, detergents, cosmetics, and pharmaceuticals (49).

HMHEC is a modification with low levels of much longer hydrocarbon chains (hydrophobes) that not only increase surface activity but also impart associative behavior to HEC; this produces dramatic effects on solution viscosity and rheology (37,74). For example, a HEC with a 2° o solution viscosity of 10 mPa·s(cP) modified with ~2.5 wt % of a C₁₄-chain hydrocarbyl moiety has a viscosity of 800 mPa·s(cP). The effect has been attributed to micellar aggregation of the hydrophobic groups in solution (37–39). The solubility and rheological properties of HMHEC depend primarily on the molecular weight, the DS and chain length of the hydrophobe, the polymer concentration, and the composition of the aqueous media. It has been found that HMHEC is an efficient rheology control agent in latex paints (39,74). Typical properties of a HMHEC are given in Table 7.

METHYLCELLULOSE AND ITS MIXED ETHERS

Properties. Methylcellulose [9004-67-5] (MC) and its alkylene oxide derivatives hydroxypropylmethylcellulose [9004-65-3] (HPMC), hydroxyethylmethylcellulose [9032-42-2] (HEMC), and hydroxybutylmethylcellulose [9041-56-9] (HBMC) are nonionic, surface-active, water-soluble polymers. Each type of derivative is available in a range of methyl and hydroxyalkyl substitutions. The extent and uniformity of the methyl substitution and the specific type of hydroxyalkyl substituent affect the solubility, surface activity, thermal gelation, and other properties of the polymers in solution.

These four methylcelluloses are available in a range of substitutions.

	Methyl DS	Hydroxyalkyl MS
methylcellulose	1.4–2.0	
hydroxypropylmethylcellulose	1.1–2.0	0.1–1.0
hydroxyethylmethylcellulose	1.3–2.2	0.06–0.5
hydroxybutylmethylcellulose	<1.9	<0.04

Methylcellulose with a methyl DS less than about 0.6 is alkali-soluble. From about 1.6 to 2.4, it is water-soluble (most commercial grades); above 2.4, it is soluble in a wide variety of organic solvents. Methylcellulose solutions in water start to gel at ~55°C, independent of molecular weight. The gelation is a function of the DS, rate of heating, and type and amounts of additives such as salts. As the temperature increases, the viscosity initially decreases (typical behavior). When the gelling temperature is reached, the viscosity sharply rises until the flocculation temperature is reached. Above this temperature, the viscosity collapses. This process is reversible with temperature (75).

The mixed derivatives HEMC, HPMC, and HBMC tend to precipitate rather than gel as the temperature is increased. The higher the hydroxyalkyl substitution, the greater the tendency for precipitation. HEMCs and HPMCs tend to have higher gelation and flocculation temperatures (75). The mixed derivatives are generally more tolerant of added salts than methylcellulose itself. HPMC and HBMC are tolerant of and are soluble in some organic solvents, especially lower alcohols and glycols.

Solutions of methylcelluloses are pseudoplastic below the gel point and approach Newtonian flow behavior at low shear rates. Above the gel point, solutions are very thixotropic because of the formation of three-dimensional gel structure. Solutions are stable between pH 3 and 11; pH extremes will cause irreversible degradation. The high substitution levels of most methylcelluloses result in relatively good resistance to enzymatic degradation (16).

Methylcellulose and its mixed ethers are surface-active cellulose ethers having surface tension values as low as 44 mN m(dyn cm) and interfacial tension values as low as 17 mN m(dyn cm) against paraffin oil.

Typical properties of MC, HPMC, HEMC, and HBMC are given in Table 8.

Table 8. Typical Properties of Methylcellulose Ethers^a

Property	MC	HPMC	HEMC	HBMC
	<i>Powder</i>			

appearance	white	white	white	white
bulk density, g cm ³		0.25–0.70		
volatiles, %		8 max		
ash content (as Na ₂ SO ₄), %		2.5 max		
	<i>Solution</i>			
viscosity ^b , mPa·s(cP)	10–15,000	5–70,000	100–70,000	
sp gr, 20° at 20°C		1.0032		
pH, 1%		5.5–9.5		
surface tension, 0.1% , mN m(dyn cm)	47–53	44–56	46–53	49–55
interfacial tension ^c , mN m(dyn cm)	19–23	17–30	17–21	20–22
gelation temp, °C	48	54–70		49
flocculation temp, °C	50–75	60–90	60–90	
	<i>Film</i>			
tensile strength, MPa ^d , 50% rh	58.6–78.6	58.6–61		
elongation, %, 50% rh	10–15	5–10		
softening point, °C		240		
melting point, °C	290–305	260		
vapor transmission, nmol (m·s) ^e				
water, 37°C, 90–100% rh		520		
oxygen, 24°C		560		

^a Refs. 42, 43.

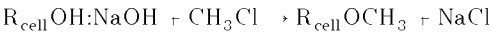
^b 2% Solution, Brookfield, 20 rpm.

^c Against paraffin oil.

^d To convert MPa to psi, multiply by 145.

^e To convert nmol (m·s) to $\frac{\text{g}\cdot\text{mil}}{100\text{ in.}^2\cdot\text{d}}$ for water, multiply by 3.95; for O₂, by 7.02.

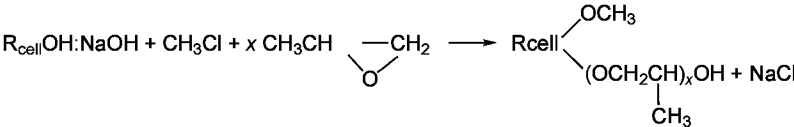
Manufacture. Methylcellulose is manufactured by the reaction of alkali cellulose with methyl chloride (76).



The reaction is accompanied by side reactions that lead to methanol and dimethyl ether by-products.



Hydroxyalkyl modification is made by simultaneous or staged addition of an alkylene oxide, as exemplified in the following (77–79).



Similarly, ethylene oxide and 1,2-butylene oxide are used to make methylhydroxy-ethylcellulose and methylhydroxybutylcellulose, respectively.

Unlike HEC and CMC, which are purified by washing with aqueous organic solvents, methylcellulose and its hydroxyalkyl modifications are purified in hot water where they are insoluble. As with other cellulose ethers, drying and grinding complete the process.

Economic Aspects. A breakdown of salient figures in 1987 for the methylcelluloses is given in Table 9. The Dow Chemical Company is the only U.S. manufacturer. They produce and market methyl- (MC), hydroxypropylmethyl-(HPMC), and hydroxybutylmethyl- (HBMC) celluloses. European producers include Aqualon Co. in Germany and Belgium, Hoechst AG in Germany, Dow Chemical GmbH in Germany, Wolff Walsrode AG in Germany, and Courtaulds Fibres Ltd. in the United Kingdom. Shin-Etsu Chemical Co., Ltd. and Matsumoto Yushi-Seiyaku Co., Ltd. are the two Japanese manufacturers.

Table 9. Worldwide Supply and Demand for Methylcelluloses^a, 10³t

Region	Capacity	Production	Consumption	Imports	Exports
United States	22	16	16	1	2
Western Europe	51	44	35.5		
Japan	7	7	5		2
Canada, Latin America, other Asia					
<i>Total</i>	<i>80</i>	<i>67</i>	<i>62</i>		

^a In 1987 (1).

Specifications and Standards; Test Methods. Premium grades of methylcellulose meet the requirements of U.S.P. XIX and *Food Chemicals Codex II*, and the *International Codex Alimentarius*. They are GRAS, meeting the requirements of Food Additives Regulation 182.1480 as multiple purpose food substances for nonstandardized foods. Premium grades of some hydroxypropylmethylcelluloses meet requirements of U.S.P. XIX, *Food Chemicals Codex II*, and Food Additives Regulation 172.874, which allows their use in nonstandardized foods. Methylcellulose and hydroxypropylmethylcellulose qualify as inert ingredients under CRF 180.1000 that may be used in formulations applied to growing crops or raw agricultural commodities after harvest.

Analytical procedures and test methods are described in manufacturers' technical bulletins (42,43).

Uses. There are numerous applications for methylcellulose and its derivatives. Some important ones are summarized in Table 10.

Table 10. Applications for Methylcellulose and its Derivatives^a

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Industry	Application	Function
construction	cements, mortars	thickener, water-binder, workability
foods	mayonnaise, dressing	stabilizer, emulsifier
	desserts	thickener
pharmaceuticals	tablets	binder, granulation aid
	formulations	stabilizer, emulsifier
adhesives	wallpaper paste	adhesive
ceramics	slip casts	binder (promotes green strength)
coatings	latex paints	thickener
	paint removers	thickener
cosmetics	creams, lotions	stabilizer, thickener

^a Refs. 42, 43.

ETHYLCELLULOSE AND HYDROXYETHYLETHYLCELLULOSE

Properties. Ethyl cellulose [9004-57-3] (EC) is a nonionic, organo-soluble, thermoplastic cellulose ether, having an ethyl DS in the range of ~2.2–2.7. Actually, EC is water-soluble at DS ~1.2, but only those products that are thermoplastic and soluble in organic solvents are of commercial importance, because of their ability to form tough, stable films. Above a DS of about 2.5, EC is soluble in many nonpolar solvents.

Film mechanical properties, such as tensile strength, elongation, and flexibility, depend more on the molecular weight (degree of polymerization) than on substitution. Elongation and tensile strength increase to a maximum with increasing molecular weight; flexibility increases linearily.

Ethylcellulose is subject to oxidative degradation in the presence of sun- or ultraviolet light, especially at elevated temperatures above the softening point. It must, therefore, be stabilized with antioxidants (44). EC is stable to concentrated alkali and brines but is sensitive to acids.

Organo-soluble hydroxyethylethylcellulose (HEEC) is highly ethoxylated with small amounts of hydroxyethyl substitution. It is used in coating applications that require solubility in fast-drying aliphatic hydrocarbons. These EHEC polymers are the only commercially available cellulosic polymers substantially soluble in low cost, low odor aliphatic hydrocarbon solvents. As a result, formulation costs are lowered and application conditions are simplified. Like ethylcellulose, HEEC is subject to oxidative degradation by the combination of heat and light (45). Degradation is more rapid above the melting point (175°C). An antioxidant, such as octylphenol, combined with an acid acceptor, such as an epoxy resin, provides protection against heat degradation. Benzophenone derivatives provide protection against sunlight. Primary uses for organic solvent-soluble EHECs are as additives in printing inks, clear lacquers, and other coatings such as alkyd, flat, and semigloss finishes. Table 11 gives typical properties for EC and HEEC.

Table 11. Typical Properties of EC and HEEC^a

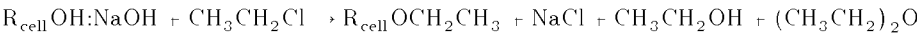
Property	EC	HEEC
	<i>Powder</i>	
appearance	white	white
volatiles, %	2	
bulk density, g cm ³	0.3–0.35	0.3–0.35
softening point, °C	152–162	
	<i>Film</i>	
specific gravity	1.140	1.120
refractive index	1.470	1.47
tensile strength, MPa ^b	46–72	34–41
elongation, %	7–30	6–10
flexibility ^c	160–2000	500–900
dielectric constant, 60 Hz	2.5–4.0	

^a Refs. 44, 46.

^b To convert mPa to psi, multiply by 145.

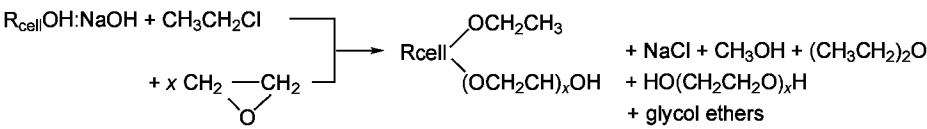
^c MIT double folds.

Manufacture. Ethyl chloride undergoes reaction with alkali cellulose in high pressure nickel-clad autoclaves. A large excess of sodium hydroxide and ethyl chloride and high reaction temperatures (up to 140°C) are needed to drive the reaction to the desired high DS values (>2.0). In the absence of a diluent, reaction efficiencies in ethyl chloride range between 20 and 30%, the majority of the rest being consumed to ethanol and diethyl ether by-products.



Higher ethyl chloride efficiency is claimed for a process utilizing a hydrocarbon diluent coupled with stepwise addition of sodium hydroxide (80). Product work-up includes distillation to remove residual unreacted ethyl chloride, added diluent, methanol, and diethyl ether; neutralization of excess sodium hydroxide; washing in water to remove salts; drying; and grinding.

The manufacturing process for organo-soluble EHEC is similar to that for EC except that alkali cellulose reacts first with ethylene oxide to a low hydroxyethyl MS value of ~0.5 at a low temperature, ~50°C, followed by reaction of the ethyl chloride at a higher temperature. Additional by-products, which are removed during purification, include glycols and the reaction products of the glycols with ethyl chloride (glycol ethers).



Economic Aspects. The Dow Chemical Company and Aqualon Co. are the only listed principal producers of EC and HEEC products worldwide. Consumption has remained constant over the past several years, and the products are not expected to grow in the future. Production is estimated at 5000 t yr, roughly equally divided between The Dow Chemical Company and Aqualon Co. As with other cellulose ethers, the price for EC and HEEC varies by grade.

Specifications and Standards; Test Methods. Ethylcellulose is cleared for many applications in food and food contact under the Federal Food, Drug, and Cosmetic Act, as amended. Examples include binder in dry vitamin preparations for animal feed, coatings and inks for paper and paperboard products used in food packaging, and closures with sealing gaskets for food containers (44). Methods of analyses are given in ASTM D914-72 (19), *National Formulary XIV*, and *Food Chemicals Codex II*.

Uses. A summary of the applications for ethylcellulose is given in Table 12.

Table 12. Applications for EC and HEEC^a

Industry	Application	Function
coatings	lacquers, varnishes	protective film-former, additive to increase film toughness and durability, shorten drying time
printing	inks	film-former
adhesives	hot melts	additive to increase toughness

^a Refs. 44, 46.

HYDROXYPROPYLCELLULOSE

Properties. Hydroxypropylcellulose [9004-64-2] (HPC) is a thermoplastic, nonionic cellulose ether that is soluble in water and in many organic solvents. HPC combines organic solvent solubility, thermoplasticity, and surface activity with the aqueous thickening and stabilizing properties characteristic of other water-soluble cellulosic polymers described herein. Like the methylcelluloses, HPC exhibits a low critical solution temperature in water.

The substitution of HPC is defined by the MS. Molar substitutions higher than approximately 3.5 are needed for solubility in water and organic solvents.

HPC is available in a number of viscosity grades, ranging from about 3000 mPa·s(–cP) at 1% total solids in water to 150 mPa·s(–cP) at 10% total solids. HPC solutions are pseudoplastic and exceptionally smooth, exhibiting little or no structure or thixotropy. The viscosity of water solutions is not affected by changes in pH over the range of 2 to 11. Viscosities decrease as temperature is increased. HPC precipitates from water at temperatures between 40 and 45°C. Dissolved salts and other compounds can profoundly influence the precipitation temperature (50,81).

HPC is compatible with many natural and synthetic water-soluble polymers and gums (50). Generally, blends of HPC with another nonionic polymer such as HEC yield water solutions having viscosities in agreement with the calculated value. Blends of HPC and anionic CMC, however, produce solution viscosities greater than calculated. This synergistic effect may be reduced in the presence of dissolved salts or if the pH is below 3 or above 10.

Like the methylcelluloses, water solutions of HPC display greatly reduced surface tension. A 0.1% solution of HPC at 25°C has a surface tension of about 44 mN/m(–dyn/cm) (water is 74.1 mN/m) and interfacial tension of about 12.5 mN/m(–dyn/cm) against mineral oil. The molecular weight of the HPC has only a slight effect on the surface tension.

Examples of polar organic solvents that dissolve HPC are methanol, ethanol, propylene glycol, and chloroform. There is no tendency for HPC to precipitate as the temperature is raised. In fact, elevated temperatures improve the solvent power of organic liquids.

Some typical properties of commercial HPC are given in Table 13.

Table 13. Typical Properties of HPC^a

Property	Value
<i>Powder</i>	
appearance	off-white
volatiles, %	5 max
ash content (as Na ₂ SO ₄), %	0.2–0.5
softening point, °C	100–150
molecular weight, <i>M_w</i>	8.0 × 10 ⁴ –1.15 × 10 ⁶
<i>Solution</i>	
viscosity, Brookfield, 30 rpm, mPa·s(–cP)	
at 1% (high <i>M_w</i>)	2500
at 10% (low <i>M_w</i>)	100
surface tension, 0.1%, mN/m(–dyn/cm)	43.6
interfacial tension ^b , 0.1%, mN/m	12.5
<i>Film</i>	
tensile strength, MPa ^c	14
elongation, %	50
flexibility ^d (50 μm film)	10,000
refractive index	1.559

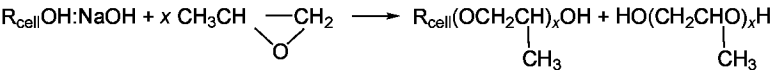
^a Ref. 50.

^b Against mineral oil.

^c To convert MPa to psi, multiply by 145.

^d MIT double folds.

Manufacture. HPC is manufactured by reaction of propylene oxide [75-56-9] with alkali cellulose.



The reaction may be conducted in stirred autoclaves in the presence of hydrocarbon diluents (82,83). Like the methylcelluloses, advantage is taken of the low critical solution temperature of HPC and it is purified through multiple washings with hot water. Consequently, very low levels of residual salts and by-products are present in the final products.

Economic Aspects. The Aqualon Co. is the only U.S. manufacturer. It is also produced in Japan by Nippon Soda Co., Ltd. Worldwide consumption in 1987 was estimated at 2300 metric tons.

Specifications and Standards; Test Methods. Food-grade HPC products are manufactured for use in food and conform to the specifications for HPC set forth in CFR 21, Section 172.870. Food grades of HPC also conform to the specifications for HPC as listed in the current edition of the *Food Chemicals Codex*.

Pharmaceutical and cosmetic grades of HPC, as for example Klucel NF manufactured by Aqualon Co., conform to the requirements of the HPC monograph as listed in the current edition of the *National Formulary*.

Toxicity testing indicates that HPC is physiologically inert (50).

Procedures for determining the ash content and moisture level, solution preparation, and viscosity measurement techniques are given in the manufacturer's literature (50).

Uses. A summary of significant uses for HPC is given in Table 14.

Table 14. Applications for HPC^a

Industry	Application	Function
polymerization	PVC suspension polymerization	protective colloid
pharmaceutical	tablets	binder, film-former
coatings	paint remover	thickener
foods	whipped toppings	stabilizer
	processed foods	extrusion aid
ceramics	slip casts	binder (promotes green strength)

^a Ref. 50.

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CEMENT

The term cement is used to designate many different kinds of substances that are used as binders or adhesives (qv). The cement produced in the greatest volume and most widely used in concrete for construction is Portland cement. Masonry and oil well cements are produced for special purposes. Calcium aluminate cements are extensively used for refractory concretes (see ALUMINUM COMPOUNDS, ALUMINUM OXIDE; REFRACTORIES). Such cements are distinctly different from epoxies and other polymerizable organic materials. Portland cement is a hydraulic cement, ie, it sets, hardens, and does not disintegrate in water. Hence it is suitable for construction of underground, marine, and hydraulic structures whereas gypsum plasters and lime mortars are not. Organic materials, such as latexes and water-soluble polymerizable monomers, are sometimes used as additives to impart special properties to concretes or mortars; furthermore, concretes are sometimes impregnated with liquid organic monomers (or liquid sulfur) and polymerized to produce polymer-impregnated concrete. The term cements as used herein is confined to inorganic hydraulic cements, principally Portland and related cements. The essential feature of these cements is the ability on hydration to form with water relatively insoluble bonded aggregations of considerable strength and dimensional stability (see also BUILDING MATERIALS, SURVEY).

Hydraulic cements are manufactured by processing and proportioning suitable raw materials, burning (or clinkering at a suitable temperature), and grinding the resulting hard nodules called clinker to the fineness required for an adequate rate of hardening by reaction with water. Portland cement consists mainly of tricalcium silicate [12168-85-3], Ca_3SiO_5 , and dicalcium silicate [10034-77-2], Ca_2SiO_4 . Usually two types of raw materials are required: one rich in calcium, such as limestone, chalk, marl, or oyster or clam shells; the other rich in silica, such as clay or shale. The two other significant phases in Portland cements are tricalcium aluminate [12042-78-3], $\text{Ca}_3\text{Al}_2\text{O}_6$, and ferrite phase (see FERRITES). A small amount of calcium sulfate [7778-18-9], CaSO_4 , in the form of gypsum or anhydrite is also added during grinding to control the setting time and enhance strength development (see CALCIUM COMPOUNDS, CALCIUM SULFATE).

The demand for cement was stimulated by the growth of canal systems in United States during the nineteenth century. Process improvements were made in the calcination of certain limestones for the manufacture of natural cements, which were gradually displaced by Portland cement. This latter was named in a 1824 patent because of its color and resemblance to a natural limestone quarried on the Isle of Portland in England. Research conducted since that time has provided a clear picture of the composition, properties, and fields of stability of the principal systems found in Portland cement. These results led to the widely used Bogue calculation of composition based on oxide analysis (1). Details beyond the scope of this article may be found in the literature (2).

Clinker Chemistry

The conventional cement chemists' notation uses abbreviations for the most common constituents: calcium oxide [1305-78-8], CaO , = C; silicon dioxide [7631-86-9], SiO_2 = S; aluminum oxide [1344-28-1], Al_2O_3 = A; ferric oxide [1309-37-1], Fe_2O_3 , = F; magnesium oxide [1309-48-4], MgO , = M; sulfur trioxide [7446-11-9], SO_3 , = $\overline{\text{S}}$; sodium oxide [1313-59-3], Na_2O , = N; potassium oxide [12136-45-7], K_2O , = K; carbon dioxide, CO_2 , = $\overline{\text{C}}$; and water, H_2O , = H. Thus tricalcium silicate, Ca_3SiO_5 , is denoted by C_3S .

Portland cement clinker is formed by the reactions of calcium oxide and acidic components to give C_3S , C_2S , C_3A , and a ferrite phase approximating C_4AF .

Phase Equilibria. During burning in the kiln, about 20–30% of liquid forms in the mix at clinkering temperatures. Reactions occur at surfaces of solids and in the liquid. The crystalline silicate phases formed are separated by the interstitial liquid. The interstitial phases formed from the liquid in normal clinkers during cooling are also completely crystalline to x-rays, although they may be so finely subdivided as to appear glassy (optically amorphous) under the microscope.

The high temperature phase equilibria governing the reactions in cement kilns have been studied, eg, in the $\text{CaO}-\text{Al}_2\text{O}_3-\text{SiO}_2$ system illustrated in Figure 1. In such a ternary diagram, the primary-phase fields are plotted, ie, the composition regions in which any one solid is the first to separate when a completely liquid mix is cooled to produce negligible supercooling. The primary-phase fields are separated by eutectic points on the sides of the triangle such as that at 1436°C between tridymite and α -CS.

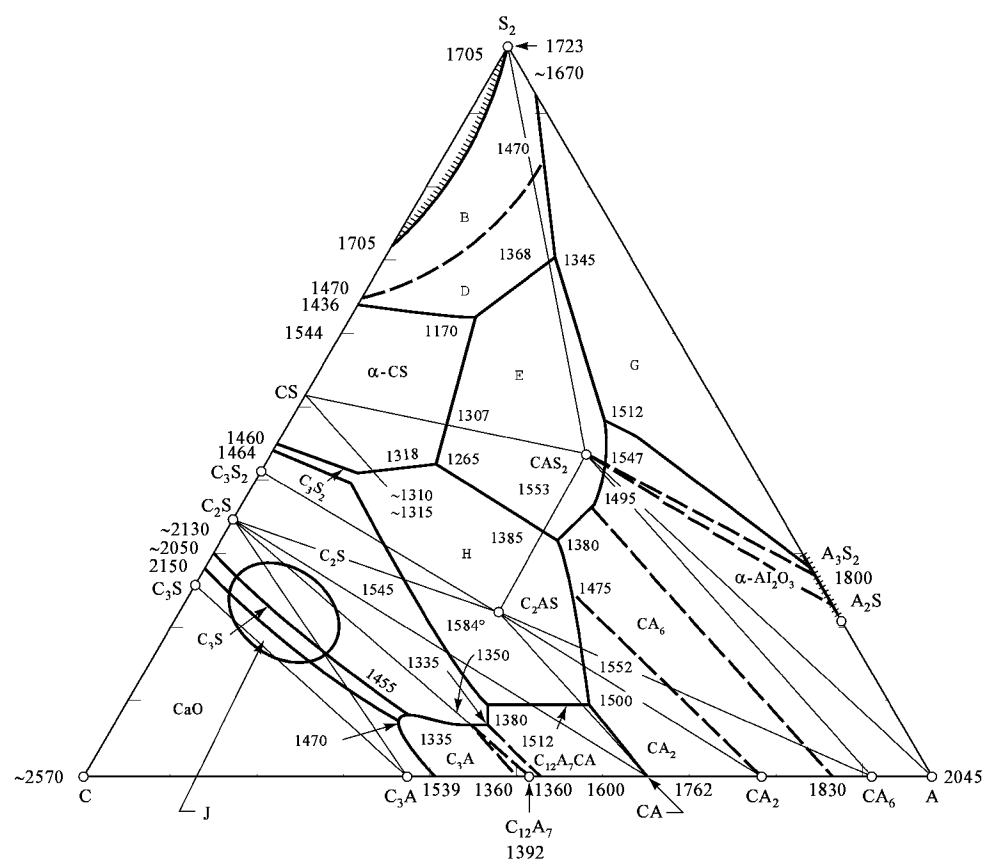


Fig. 1. Phase equilibria in the C-A-S ($\text{CaO}-\text{Al}_2\text{O}_3-\text{SiO}_2$) system (3,4); temperatures are in $^{\circ}\text{C}$. Shaded areas denote two liquids; compositional index marks on the triangle are indicated at 10° intervals; **B** denotes cristobalite [14464-46-1], and **D** denotes tridymite [15468-32-3], both of SiO_2 composition; **E** is anorthite [1302-54-1], $\text{Al}_2\text{CaSi}_2\text{O}_8$; **G** is mullite [55964-99-3]; **H**, gehlenite [1302-56-3], $\text{Ca}_2\text{Al}_2\text{SiO}_7$; and **J** is the area of Portland cement compositions.

In the relatively small Portland cement zone almost all modern cements fall in the high lime portion (about 65° CaO). Cements of lower lime content tend to be slow in hardening and may show trouble from dusting of the clinker by transformation of β - to γ - C_2S , especially if clinker cooling is very slow. The zone is limited on the high lime side by the need to keep the uncombined CaO to low enough values to prevent excessive expansion from hydration of the free lime. Commercial manufacture at compositions near the $\text{CaO}-\text{SiO}_2$ axis can present difficulties. If the lime content is high, the burning temperatures may be so high as to be impractical. If the lime content is low, the burning temperatures may even be low, but impurities must be present in the C_2S to prevent dusting. On the high alumina side the zone is limited by excessive liquid-phase formation which prevents proper clinker formation in rotary kilns.

The relations between the compositions of Portland cements and some other common hydraulic cements are shown in the $\text{CaO}-\text{SiO}_2-\text{Al}_2\text{O}_3$ phase diagram of Figure 2 (5). In this diagram, Fe_2O_3 has been combined with Al_2O_3 to yield the Al_2O_3 content used. This is a commonly applied approximation that permits a two-dimensional representation of the real systems.

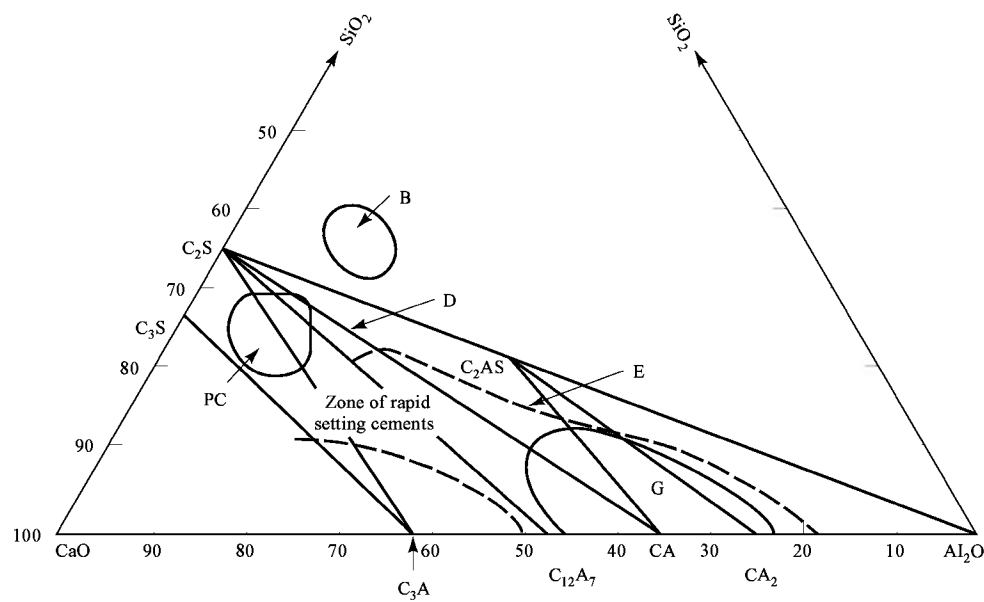


Fig. 2. Cement zones in the $\text{CaO}-\text{Al}_2\text{O}_3-\text{SiO}_2$ system (5) where **B** represents basic blast-furnace slag; **D**, cement compositions which dust on cooling; **E**, compositions showing no tendency to set; **G**, aluminous cement; and **PC**, Portland cement.

Clinker Formation. Portland cements are ordinarily manufactured from raw mixes including components such as calcium carbonate, clay or shale, and sand. As the temperature of the materials increases during their passage through the kiln, the following reactions occur: evaporation of free water; release of combined water from the clay; decomposition of magnesium carbonate; decomposition of calcium carbonate (calcination); and combination of the lime and clay oxides. The course of these last reactions (6) which occur at the high temperature end of the kiln, just before and in the burning zone, is illustrated graphically in Figure 3 (7).

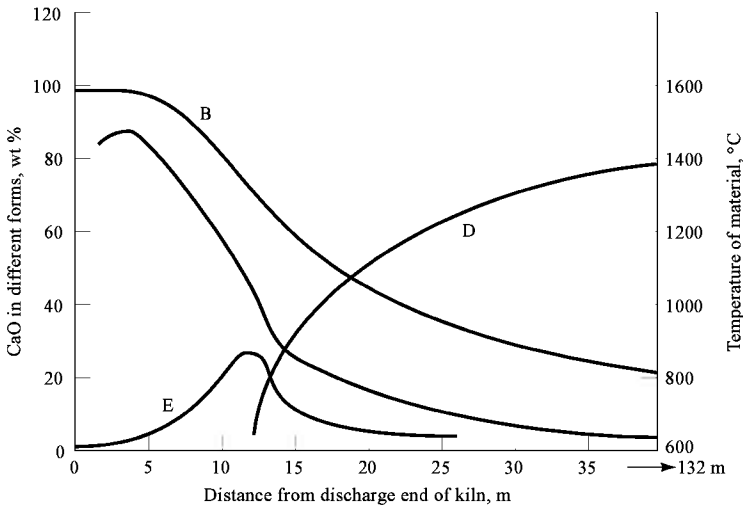


Fig. 3. Temperatures and progress of reactions in a 132-meter wet-process kiln; area B represents CaO in new compounds; D, CaO as CaCO₃; and E, free CaO.

From the phase diagram of the CaO–SiO₂–Al₂O₃ system, the sequence of crystallization during cooling of the clinker can be derived if the cooling is slow enough to maintain equilibrium. For example, a mix at 1500°C of relatively low lime content, along the C₃S–C₂S eutectic line in Figure 1, is composed of solid C₃S and C₂S and a liquid along the C₃S–C₂S eutectic at the intersection with the 1500°C isotherm to the left of the 1470–1455 line. Upon cooling, this liquid deposits more C₃S and C₂S, moving the liquid composition down to the invariant point at 1455°C, at which C₃A also separates until crystallization is complete. Although real cement clinkers contain more components, which alter the system and temperatures somewhat, the behavior is similar.

Cooling is ordinarily too rapid to maintain the phase equilibria. In the case in Figure 1, the lime-deficient liquid at 1455°C requires that some of the solid C₃S redissolve and that more C₂S crystallize during crystallization of the C₃A. During rapid cooling there may be insufficient time for this reaction and the C₃S content is thus higher than when equilibrium conditions prevail. In this event crystallization is not completed at 1455°C, but continues along the C₃A–C₂S boundary until the invariant point at 1335°C is reached. Crystallization of C₂S, C₃A, and C₁₂A₇ then occurs to reach complete solidification. Such deviations from equilibrium conditions cause variations in the phase compositions that are estimated from the Bogue calculation, and cause variations in the amounts of dissolved substances such as MgO, alkalies, and the alumina content of the ferrite phase.

The theoretical energy requirement for the burning of Portland cement clinker can be calculated from the heat requirements and energy recovery from the various stages of the process. Knowledge of the specific heats of the various phases, and the heats of decomposition, transformation, and reaction then permits calculation of the net theoretical energy requirement of 1760 kJ (420 kcal) for 1 kg of clinker from 1.55 kg of dry CaCO₃ and kaolin (see CLAYS) (8).

The kinetics of the reactions are strongly influenced by the temperature, mineralogical nature of the raw materials, fineness to which the raw material is ground, percentage of liquid phase formed, and viscosity of the liquid phase. The percentage of liquid formed depends on the alumina and iron oxides. When the sum of these oxides is low, the amount of liquid formed is insufficient to permit rapid combination of the remaining CaO. The viscosity of the liquid at clinkering temperature is reduced by increasing the amounts of oxides such as MnO, Fe₂O₃, MgO, CaO, and Na₂O (9).

The reaction of C₂S with CaO to form C₃S depends on dissolution of the lime in the clinker liquid. When sufficient liquid is present, the rate of solution is controlled by the size of the CaO particles, which depends in turn on the sizes of the particles of ground limestone. Coarse particles of silica or calcite fail to react completely under commercial burning conditions. The reaction is governed by the rate of solution (10):

$$\log t = \log \frac{D}{A} + 0.43 \frac{E}{RT}$$

t is the time in minutes, *D* is the particle diameter in mm, *A* is a constant, *T* the absolute temperature, and *E* is the activation energy having a value of 607 kJ/mol (146 kcal/mol). For example, 0.05 mm particles require 59 min for solution at 1340°C but only 2.3 min at 1450°C. A similar relation applies for the rate of solution of quartz grains.

Phases Formed in Portland Cements. Most clinker compounds take up small amounts of other components to form solid solutions (11). Best known of these phases is the C₃S solid solution called alite. Phases that may occur in Portland cement clinker are given in Table 1. In addition, a variety of minor phases may occur in Portland cement clinker when certain minor elements are present in quantities above that which can be dissolved in other phases. Under reducing conditions in the kiln, reduced phases, such as ferrous oxide [1345-25-1], FeO, and calcium sulfide [20548-54-3], CaS, may be formed.

Table 1. Phases in Portland Cement Clinker^a

Name of impure form	CAS Registry Number	Chemical name	Cement chemists' notation
free lime	[1305-78-8]	calcium oxide	C
periclase (magnesia)	[1309-48-4] and [1317-74-4]	magnesium oxide	M
alite	[12168-85-3]	tricalcium silicate	C ₃ S
belite	[10034-77-2]	dicalcium silicate	C ₂ S
C ₃ A	[12042-78-3]	tricalcium aluminate	C ₃ A
ferrite	[12612-16-7]	calcium aluminoferrite ^b	C ₂ A _x F _{1-x}
	[12068-35-8]	tetracalcium aluminoferrite	C ₄ AF
	[12013-62-6]	dicalcium ferrite ^c	C ₂ F
mayenite	[12005-57-1]	12-calcium-7-aluminate	C ₁₂ A ₇
gehlenite	[1302-56-3]	dicalcium aluminomonosilicate	C ₂ AS
aphthitalite	[12274-74-4] and [17926-93-1]	sodium, potassium sulfate ^d	N _x K _y S/ _z
arcanite	[7778-80-5] and [14293-72-2]	potassium sulfate	KS/ _z

metathenardite	[7757-82-6]	sodium sulfate form I	NS/ ^f
calcium langbeinite	[14977-32-8]	potassium calcium sulfate	2XS/ ^f KS/ ^f
anhydrite	[7778-18-9] and [14798-04-0]	calcium sulfate	CS ^ī
calcium sulfoaluminate	[12005-25-3]	tetracalcium trialuminate-sulfate	C ₄ A ₃ S ^ī
alkali belite	[15669-83-7]	α'- or β-dicalcium (potassium) silicate ^e	K _x C ₂₃ S ₁₂
alkali aluminate	[12004-54-3]	8-calcium disodium trialuminate	NC ₈ A ₃
spurrite	[65430-58-2]	5-calcium disilicate monosulfate	2C ₂ SCC/ ^f
	[1319-44-2]	5-calcium disilicate monocarbonate	2C ₂ SCC/ ^f
	[12043-73-1]	calcium aluminate chloride	C ₁₁ A ₇ CaCl ₂ ^f
	[12305-57-6]	calcium aluminate fluoride	C ₁₁ A ₇ CaF ₂ ^f

^a Refs. 12–14.
^b Solid solution series where $x = A/(A + F)$; $0 < x < 0.7$.
^c End member of series.
^d Solid solution series when $1/3 \leq x/2$.
^e Solid solution series when $x < 1$.
^f Mixed notation.

The primary phases all contain impurities. In fact these impurities stabilize the structures formed at high temperatures so that decomposition or transformations do not occur during cooling, as occurs with the pure compounds. For example, pure C₃S exists in at least six polymorphic forms each having a sharply defined temperature range of stability, whereas alite exists in three stabilized forms at room temperature depending on the impurities. Some properties of the more common phases in Portland clinkers are given in Table 2.

Table 2. Properties of the More Common Phases in Portland Cement Clinker^a

Name	Crystal system	Density, g/L	Mohs' hardness
alite	triclinic	3.14–3.25	ca 4
	monoclinic		
	trigonal		
belite	hexagonal	3.04	>4
	orthorhombic	3.40	
	monoclinic	3.28	
	orthorhombic	2.97	
C ₃ A	cubic	3.04	<6
ferrite	orthorhombic	3.74–3.77	ca 5
free lime	cubic	3.08–3.32	
magnesia	cubic	3.58	

^a Refs. 11–16.

Structure. Examination of thin sections of clinkers using transmitted light, and of polished sections by reflected light, reveals details of the structure. The polarizing microscope has been used to determine the size and birefringence of alite crystals, and the size and color of the belite to predict later age strength (17). The clinker phases are conveniently observed by examining polished sections selectively etched using special reagents as shown in Figure 4. The alite appears as clear euhedral crystalline grains, the belite as rounded striated grains, the C₃A as dark interstitial material, and the C₄AF as light interstitial material.

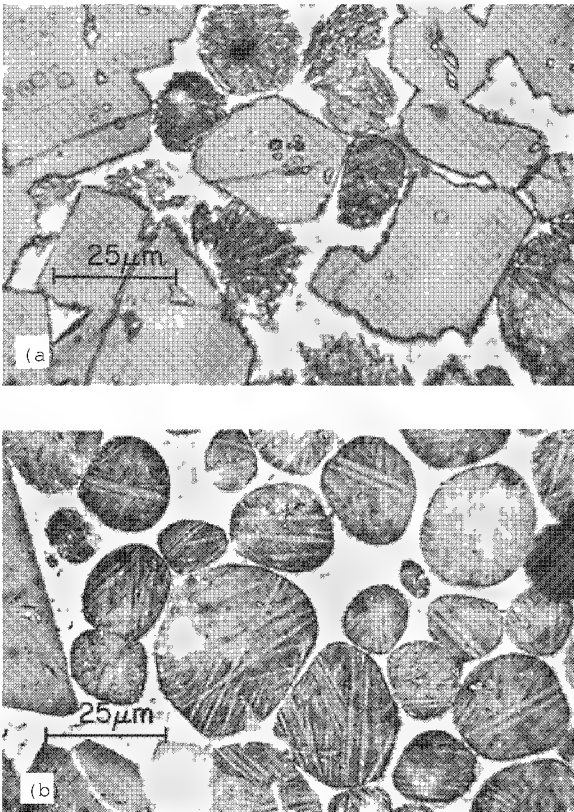


Fig. 4. Photomicrograph of polished and etched sections of Portland cement clinkers. The C₃A appears as dark interstitial material, the C₄AF as light

interstitial material. **(a)** Euhedral and subhedral alite crystals and rounded or ragged belite; **(b)** rounded and striated belite crystals.

Portland cement clinker structures (18,19) vary considerably with composition, particle size of raw materials, and burning conditions, resulting in variations of clinker porosity, crystallite sizes and forms, and aggregations of crystallites. Alite sizes range up to about 80 μm or even larger, most being 15–40 μm.

Raw Material Proportions. The three main considerations in proportioning raw materials for cement clinker are the potential compound composition; the percentage of liquid phase at clinkering temperatures; and the burnability of the raw mix, ie, the relative ease, in terms of temperature, time, and fuel requirements, of combining the oxides into good quality clinker. The ratios of the oxides are related to clinker composition and burnability. For example, as the CaO content of the mix is increased, more C₃S can be formed, but certain limits cannot be exceeded under normal burning conditions. The lime saturation factor (LSF) is a measure of the amount of CaO that can be combined (20):

$$\text{LSF} = \frac{\% \text{ CaO}}{2.8 (\% \text{ SiO}_2) + 1.1 (\% \text{ Al}_2\text{O}_3) + 0.7 (\% \text{ Fe}_2\text{O}_3)}$$

An LSF of 100 would indicate that the clinker can contain only C₃S and the ferrite solid solution. Lime saturation factors of 88–94 are frequently appropriate for reasonable burnability; low LSF indicates insufficient C₃S for acceptable early strengths, and higher values may render the mix very difficult to burn. Several other weight ratios such as the silica modulus and the iron modulus are also important (21).

The potential liquid-phase content at clinkering temperatures range from 18 to 25% and can be estimated from the oxide analysis of the raw mix. For example (22), for 1450°C:

$$\% \text{ liquid phase} = 1.13 (\% \text{ C}_3\text{A}) + 1.35 (\% \text{ C}_4\text{AF}) + \% \text{ M} + \% \text{ alkalis}$$

The potential compound composition of a cement or cement clinker can be calculated from the oxide analyses of any given raw materials mixture, or from the oxide analyses of the cement clinker or finished cement. The simplest and most widely used method is the Bogue calculation (23). The ASTM C150 (24) calculation is somewhat modified.

The techniques of determining the proper proportions of raw materials to achieve a mix of good burnability and clinker composition may be determined by computer using an iterative program, starting with raw components of known composition. The concept of targets may be utilized, including fixed values of moduli, compound content, and amount of any raw material element in the final clinker. The number of targets that may be set is one less than the number of raw materials. The fuel ash must be considered as one of the raw materials. Representative chemical analyses of raw materials used in making Portland and high alumina cements are given in Table 3, analyses of cements of various types appear in Table 4, and their potential compound compositions in Table 5.

Table 3. Chemical Composition of Raw Materials^a, wt %

Type	SiO ₂	Al ₂ O ₃	Fe ₂ O ₃	CaO	MgO	Loss on ignition
cement rock	13.4	3.5	1.7	42.9	1.0	37.2
limestone	1.2	0.2	0.4	53.4	1.3	43.4
dolomite	4.5	0.5	1.6	35.0	14.9	44.0
marl	6.0	0.6	2.3	49.1	0.4	40.4
oyster shells	1.5	0.4	1.2	52.3	0.7	41.8
shale	53.8	18.9	7.7	3.2	2.2	8.2
clay	67.8	14.3	4.5	0.9	1.2	8.0
mill scale			ca 100.0			
sandstone	76.6	5.3	3.1	4.7	1.7	6.6
bauxite	10.6	57.5	2.6			28.4

^a Courtesy of the American Concrete Institute (25).

Table 4. Chemical Composition of Cements, wt %

	SiO ₂	Al ₂ O ₃	Fe ₂ O ₃	CaO	MgO	SO ₃	Loss of ignition	Insoluble residue
Type I	20.9	5.2	2.3	64.0	2.8	2.9	1.0	0.2
Type II	21.7	4.7	3.6	63.6	2.9	2.4	0.8	0.4
Type III	21.3	5.1	2.3	64.9	3.0	3.1	0.8	0.2
Type IV	24.3	4.3	4.1	62.3	1.8	1.9	0.9	0.2
Type V	25.0	3.4	2.8	64.4	1.9	1.6	0.9	0.2
white	24.5	5.9	0.6	65.0	1.1	1.8	0.9	0.2
alumina	5.3	39.8	14.6	33.5	1.3	0.4	0	4.8

Table 5. Potential Compound Composition of Cements^a, wt %

	C ₃ S	C ₂ S	C ₃ A	C ₄ AF
Type I	55	19	10	7
Type II	51	24	6	11
Type III	56	19	10	7
Type IV	28	49	4	12
Type V	38	43	4	9
white	33	46	14	2

^a Calculated by the American Society for Testing and Materials C150-76 (24). In cement chemists' notation.

Hydration

Calcium Silicates. Cements are hydrated at elevated temperatures for the commercial manufacture of concrete products. Using low pressure steam curing or hydrothermal treatment above 100°C at pressures above atmospheric, the products formed from calcium silicates are often the same as the hydrates formed from their oxide constituents. Hence lime and silica are frequently used in various proportions with or without Portland cement in the manufacture of calcium silicate hydrate products. Some of these compounds are listed in Table 6.

Table 6. Calcium Silicate Hydrates Formed at Elevated Temperatures^a

Name	CAS Registry Number	Composition ^b	Tempera-ture of formation, °C	Density, kg m ⁻³
tricalcium silicate hydrate	[54596-90-6]	C ₃ S ₂ H ₃	150–500	2.61
calciochondrodite	[12141-47-8]	C ₅ S ₂ H	250–800	2.84
dicalcium silicate hydrate				
α (A)	[15630-58-7]	C ₂ SH	100–200	2.8
β (B)	[18536-02-2]	C ₂ SH	140–350	2.66
γ (C) ^c	[15669-77-9]	(C ₆ S ₂ H + C ₃ S ₂ H _x ?)	160–300	2.67
δ (D)	[54694-02-9]	C ₃ S ₃ H	350–800	2.98
afwillite	[16291-79-5]	C ₃ S ₂ H ₃	100–160 ^d	2.63
foshagite	[12173-33-0]	C ₄ S ₃ H	300–500	2.7
	[62520-56-3]			
xonotlite	[12141-77-4]	C ₅ S ₅ H	150–400	2.7
C–S–H (II)		C _{1.5–2.0} SH _x	<100	2.0–2.2
C–S–H (I)		C _{0.8–1.5} SH _y	<130	
tobermorite,	[1319-31-9]	C ₅ S ₅ H ₉	60(?)	2.2
1.4 nm	[1344-96-3]			
1.13 nm	[12028-62-5]	C ₅ S ₅ H ₅	110–140	2.44
	[12323-54-5]			
0.93 nm	[51771-55-2]	C ₅ S ₅ H	250–450	2.7
gyrolite	[16225-87-9]	C ₂ S ₃ H ₂	120–200	2.39
	[12141-71-8]			
	[60385-01-5]			
truscottite	[12425-42-2]	C ₃ S ₁₀ H ₃	200–300	2.36–2.48

^a Refs. 12,13, and 26.

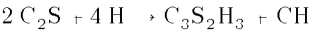
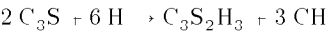
^b In cement chemists' notation, where subscripts *x* and *y* indicate variable unknown quantities.

^c Material is probably a mixture.

^d Afwillite can also be formed, and appears to be the thermodynamically stable calcium silicate hydrate in pure systems, at room temperature.

Although hydration under hydrothermal conditions may be rapid, metastable intermediate phases tend to form, and final equilibria may not be reached for months at 100–200°C, or weeks at even higher temperatures. Hence, the temperatures of formation given in Table 6 indicate the conditions under saturated steam pressure that may be expected to yield appreciable quantities of the compound, although it may not be the most stable phase at the given temperature. The compounds are listed in order of decreasing basicity, or lime–silica ratio. Reaction mixtures having ratios C : S = 1 yield xonotlite at 150–400°C. Intermediate phases of C–S–H (I), C–S–H (II), and crystalline tobermorite are formed in succession. Tobermorite (1.13 nm) appears to persist indefinitely under hydrothermal conditions at 110–140°C; it is a principal part of the binder in many autoclaved cement–silica and lime–silica products.

In hydrations at ordinary temperatures (27) pure C₃S and β-C₂S, corresponding to the alite and belite phases in Portland cements, respectively, react with water to form calcium hydroxide and a single calcium silicate hydrate (C–S–H). Using cement chemists' notation



These are the main reactions in Portland cements because the two calcium silicates constitute about 75% of the cement. The average lime–silica ratio (C:S) may vary from about 1.5 to about 2.0 or even higher, the average value is about 1.7. The water content varies with the ambient humidity, the three moles of water being estimated from measurements in the dry state and structural considerations. As the lime–silica ratio of the C–S–H increases, the amount of water increases on an equimolar basis, ie, the lime goes into the structure as calcium hydroxide, resulting in less free calcium hydroxide.

Calcium silicate hydrate is not only variable in composition, but is very poorly crystallized, and is generally referred to as calcium silicate hydrate gel or tobermorite gel because of the colloidal sizes (<0.1 μm) of the gel particles. The calcium silicate hydrates are layer minerals having many similarities to the limited swelling clay minerals found in nature. The layers are bonded together by excess lime and interlayer water to form individual gel particles only 2–3 layers thick. Surface forces, and excess lime on the particle surfaces, tend to bond these particles together into aggregations or stacks of the individual particles to form the porous gel structure.

Significant changes in the structure of the gel continue over very long periods. During the first month of hydration appreciable quantities of the dimer Si₂O₇ are formed. These are reduced by later condensation to higher polysilicates, the amount of which together with the mean length of the metasilicate chains continues to increase for at least 15 years of moist curing. In one study a mean length of 15.8 silica tetrahedra was found after such prolonged curing (28). These changes appear to have a positive effect on both strength development and reduction of drying shrinkage.

Drying and other chemical processes can have significant effects on this structure, there being loss of hydrate water as well as physically adsorbed water, and collapse of the structure to form more stable aggregations of particles (29,30).

Tricalcium Aluminate and Ferrite. The hydration of the C₃A alone and in the presence of gypsum usually produces well-crystallized reaction products that can be identified by x-ray diffraction and other methods. C₃AH₆ is the cubic calcium aluminate hydrate; C₄AH₁₉ and C₄ASiH₁₂ are hexagonal phases, the latter being commonly referred to as the monosulfate. The highly hydrated trisulfate, ettringite, occurs as needles, rods, or dense columnar aggregations. Its formation on the surfaces of anhydrous grains is responsible for the necessary retardation of hydration of the aluminates in portland cements and the expansion process in expansive cements (31).

The early calcium aluminate hydration reactions in Portland cements have been studied in simple mixtures of C₃A, gypsum, calcium hydroxide, and water (32). Figure 5 shows the progressive reaction of the gypsum, water, and C₃A as ettringite is formed, the reaction of the ettringite, calcium hydroxide, and water to form the monosulfate, and the solid of the monosulfate with C₄AH₁₉. These reactions are important in the Portland cements to control the hydration of the C₃A, which otherwise might hydrate so rapidly as to cause flash set, or premature stiffening, in fresh concrete.

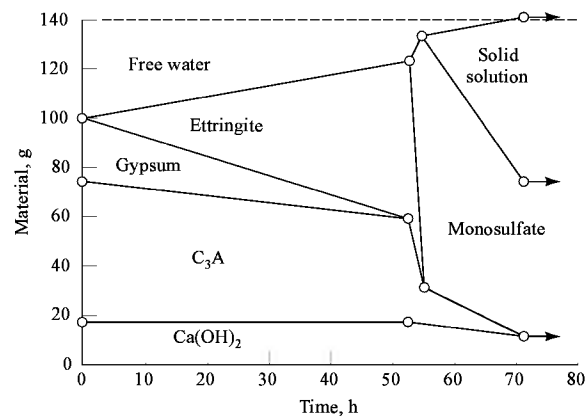


Fig. 5. The early hydration reactions of tricalcium aluminate in the presence of gypsum and calcium hydroxide. Initial molar proportions: 1-C₃A; 1-Ca(OH)₂; 3/4-CaSO₄·2H₂O; 0.4 water–solids ratio (32).

Other reactions taking place throughout the hardening period are substitution and addition reactions (29). Ferrite and sulfoferrite analogues of calcium monosulfoaluminate and ettringite form solid solutions in which iron oxide substitutes continuously for the alumina. Reactions with the calcium silicate hydrate result in the formation of additional substituted C–S–H gel at the expense of the crystalline aluminate, sulfate, and ferrite hydrate phases. The hydration of the ferrite phase (C₄AF) is of greatest interest in mixtures containing lime and other cement compounds because of the strong tendency to form solid solutions. When the sulfate in solution is very low, solid solutions are formed between the cubic C₃AH and analogous iron hydrate C₃FH. In the presence of water and silica, solid solutions such as C₃ASH₄·C₃FSH₄ may be formed (33). Table 7 lists some of the important phases formed in the hydration of mixtures of pure compounds.

Table 7. Cement Phases Hydrated at Normal Temperatures^a

Name	CAS Registry Number	Approximate composition ^b	Stability range		Crystal system	Density, kg·m ⁻³
			rh, 25°C	Temp, °C		
calcium sulfate dihydrate (gypsum)	[10101-41-4]	CS̄H ₂	100–35	<100	monoclinic	2.32
calcium hydroxide (portlandite)	[13397-24-5]	CH	100–0	<512	trigonal–hexagonal	2.24
magnesium hydroxide (brucite)	[1305-62-0]	MH	100–0	<350	trigonal–hexagonal	2.37
calcium silicate hydrate gel (C–S–H gel)	[1309-42-8]	C _x S _y H _z ^c		indefinite	indefinite	2.7 ^d
tetracalcium aluminate, 19-hydrate	[12323-54-5]	C ₄ AS̄H ₁₉	100–85	<15	trigonal–hexagonal	1.80
13-hydrate	[12042-86-3]	C ₄ AS̄H ₁₃	81–12		trigonal–hexagonal	2.02
7-hydrate	[12042-85-2]	C ₄ AS̄H ₇	2–0	to 120		
tetracalcium aluminate monosulfate, 16-hydrate	[12511-52-3]	C ₄ AS̄H ₁₆	aq	<8	trigonal–hexagonal	
14-hydrate	[67523-83-5]	C ₄ AS̄H ₁₄	100–95	>9	trigonal–hexagonal	
12-hydrate	[12421-30-6]	C ₄ AS̄H ₁₂	95–12	>1	trigonal–hexagonal	1.95
10, 8, ∞-hydrate	[12252-10-7]	C ₄ AS̄H _x	<12			
ettringite (6-calcium aluminate trisulfate, 32-hydrate)	[12252-09-4]	C ₆ AS̄ ₃ H ₃₂	100–4	<60	trigonal–hexagonal	1.73–1.79
	[12445-38-4]	C ₆ AS̄ ₃ H ₃₂	4–2	<110		
garnet-hydrogarnet solid solution series	[12252-15-2]	C ₃ (F _{1-x} AS̄ _x)(S _{1-y} H _{2y}) ₃		stable	cubic	
	[11070-82-9]	end member: C ₃ AH	100–0	>15	cubic	2.52

^a Refs. 12, 13, and 34.
^b In cement chemists' notation.
^c Where 1.3 < x/y < 2 and probably 1 < z/y < 1.5.
^d Wet.
^e $x = \frac{A}{A + F}$ and $y = \frac{2H}{2H + S}$.

Other Phases in Portland and Special Cements. In cements free lime, CaO, and periclase, MgO, hydrate to the hydroxides. The *in situ* reactions of larger particles of these phases can be rather slow and may not occur until the cement has hardened. These reactions then can cause deleterious expansions and even disruption of the concrete and the quantities of free CaO and MgO have to be limited. The soundness of the cement can be tested by the autoclave expansion test of Portland cement ASTM C151 (24). The expansive component C₄A₃S̄I in Type K expansive cements hydrates in the presence of excess sulfate and lime to form ettringite is



The reactions in the regulated-set cements containing C₁₁A₇CF₂ (note mixed notation) as a principal phase resemble those in ordinary Portland cements. Initial reaction rates are controlled by ettringite formation. Setting occurs with formation of the monosulfate, along with some transitory lower-limed calcium aluminate hydrates that convert to the monosulfate within a few hours. Pozzolans contain reactive silica which reacts with cement and water by combining with the calcium hydroxide released by the hydration of the calcium silicates to produce additional calcium silicate hydrate. If sufficient silica is added, about 30% of the weight of cement, the calcium hydroxide can

eventually be completely combined. Granulated blast-furnace slag is not ordinarily reactive in water, but in the presence of lime reactions occur with the silica framework. This breakdown of the slag releases other components so that a variety of crystalline hydrate phases can also form.

Hydration at Ordinary Temperatures. Portland cement is generally used at temperatures ordinarily encountered in construction, ie, from 5 to 40°C. Temperature extremes have to be avoided. The exothermic heat of the hydration reactions can play an important part in maintaining adequate temperatures in cold environments, and must be considered in massive concrete structures to prevent excessive temperature rise and cracking during subsequent cooling.

The initial conditions for the hydration reactions are determined by the concentration of the cement particles (0.2–100 μm) in the mixing water (0.3–0.7 on a wt % basis) and the fineness of the cement (2500–5000 cm² g). Upon mixing with water, the suspension of particles as shown in Figure 6 (35) is such that these particles are surrounded by films of water having an average thickness of about 1 μm. The anhydrous phases initially react by the formation of surface hydration products on each grain, and by dissolution into the liquid phase. The solution quickly becomes saturated with calcium and sulfate ions, and the concentration of alkali cations increases rapidly. These reactions consume part of the anhydrous grains, but the reaction products tend to fill that space as well as some of the originally water-filled space. The porous gel in its most dense configurations occupies about twice the volume of the reacted anhydrous material (36). The hydration products at this stage are mostly colloidal (<0.1 μ) but some larger crystals of calcium aluminate hydrates, sulfoaluminate hydrate, and hydrogarnets form. As the reactions proceed the coatings increase in thickness and eventually form bridges between the original grains. This is the stage of setting. Despite the low solubility and mobility of the silicate anions, growths of the silicate hydrates also form on the crystalline phases formed from the solution and become incorporated into the calcium hydroxide and other phases. Upon further hydration the water-filled spaces become increasingly filled with reaction products to produce hardening and strength development.

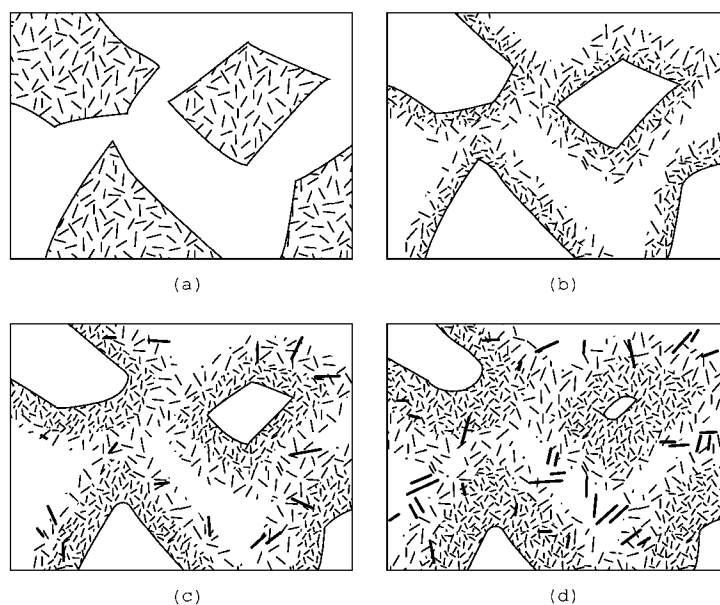
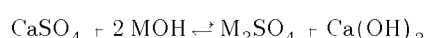


Fig. 6. Four stages in the setting and hardening of Portland cement: simplified representation of the sequence of changes. (a) Dispersion of unreacted clinker grains in water. (b) After a few minutes; hydration products eat into and grow out from the surface of each grain. (c) After a few hours; the coatings of different clinker grains have begun to join up, the gel thus becoming continuous (setting). (d) After a few days; further development of the gel has occurred (hardening).

Courtesy of Academic Press Inc. (London) Ltd. (35).

The composition of the liquid phase during the early hydration of Portland cements is controlled mainly by the solution of calcium, sulfate, sodium, and potassium ions. Very little alumina, silica, or iron are present in solution. Calcium hydroxide, as calcium oxide, and gypsum, as calcium sulfate, alone have solubilities of about 1.1 and 2.1 g L at 25°C, respectively. In the presence of alkalies released in the first 7 min, the composition tends to be governed by the equilibrium:



where M represents the alkalies. At advanced stages of hydration of low water–cement ratio pastes, the alkali solution concentration may exceed 0.4 N with a pH above 13. Saturated lime–water has a pH of 12.4 at 25°C.

The exact course of the early hydration reactions depends mainly on the C₃A, ferrite, and soluble alkali contents of the clinker, and the amount of gypsum in the cement. Following the rate of reaction by calorimetric measurements, at least two and sometimes three distinct peaks in the rate of heat liberation can be observed (33,37). A large initial peak lasts only a few minutes and may reach 6 J (gmin)(1.4 cal (gmin)) resulting mainly from the solution of soluble constituents and the surface reactions, especially the formation of the sulfoaluminate coating on the highly reactive C₃A phase. After the initial heat peak, the reactions are strongly retarded, producing a 1–2 h delay referred to as the induction period during which the cement–water paste remains plastic and the concrete is workable. The cause of the induction period is a subject of much debate. The most widely supported explanation of the induction period involves an initial reaction which forms a protective layer on the C₃S particles (38). Within 30 s, the C₃S is almost isolated from the solution. Eventually, C–S–H nucleates and grows. The protective layer is disrupted and increased access to the C₃S leads to an increasing rate of hydration which produces the second heat peak. During the second heat peak the concrete sets and establishes its familiar monolithic structure. A third heat peak may be observed depending on the gypsum and C₃A contents. If present, the third peak corresponds to the exhaustion of the solid gypsum, a rapid decrease of sulfate in solution, conversion of the ettringite to monosulfate, and renewed rapid reaction of the remaining C₃A and ferrite phases. At optimum gypsum the third peak ordinarily occurs between 18 and 24 h with maximum strength and minimum shrinkage.

In these early reactions the reactivities of the individual phases are important in determining the overall reaction rate. However, as the cement particles become more densely coated with reaction products, diffusion of water and ions in solution becomes increasingly impeded. The reactions then become diffusion-controlled at some time depending on various factors such as temperature and water–cement ratio. After about 1 or 2 days, ie, at ca 40% of complete reaction, the remaining unhydrated cement phases react more nearly uniformly.

Microscopic examination of sections of hardened cement paste show that the unhydrated cores of the larger cement particles can be distinguished from the hydrated portion or inner product, which is a pseudomorph of the original grain, and the outer product formed in the originally water-filled spaces. Measurements of these cores indicate the depth of penetration of the hydration reactions (39). The overall hydration rate increases with the temperature, the fineness of the cement, and to a lesser extent with the water–cement ratio; measurements of the activation energy indicate that the reaction becomes increasingly diffusion controlled (33). Although more finely ground cements hydrate more rapidly in the first month or more of hydration, these differences gradually disappear at later ages. After one year most Portland cements at usual water–cement ratios are more than 90% hydrated.

hydrated if continuously moist-cured. At complete hydration the chemically combined water (the water retained after strong drying) is about 20–25% of the weight of the cement, depending on its composition. However, a minimum water–cement ratio of about 0.4 is required to provide enough space to permit complete hydration of the cement (36). If moist curing is stopped and the hardened cement is dried sufficiently, eg, to 80% rh, the hydration process stops.

Cement Paste Structure and Concrete Properties

The properties of both fresh and hardened mortars and concretes depend mainly on the cement–water paste properties. Practical engineering tests are usually made using concrete specimens because their properties also depend on the proportions, size gradation, and properties of the aggregates. Quality control testing and research on cement properties is usually done on cement pastes or cement mortars made with standard sands. The properties of hardened cement pastes, mortars, and concretes are similar functions of the water–cement ratio and degree of hydration of the cement. The properties of fresh concretes that determine the workability, or ease of mixing and placement into forms, also depend strongly on, but are not so simply related to, the cement paste rheological properties (40,41).

The fresh paste even in the dormant period is normally thixotropic, or shear thinning, indicating that the structure is being continuously broken down and reformed during mixing. It is an approximately Bingham plastic body having a finite yield value and plastic viscosity from 5000 to 500 mPas(cP) as the water–cement ratio increases from 0.4 to 0.7 (42). The viscosity and yield values can be greatly reduced by the addition of certain organic water-reducing admixtures especially formulated for this purpose. Workability of concrete is measured by the slump of the concrete determined after removal of a standard slump cone (305 mm high) (43). Workable concretes have slumps of 75 mm or more.

After mixing and casting, sedimentation of the cement particles in the water results in bleeding of water to the top surface and reduction of water–cement ratio in the paste. At high water–cement ratios, some of the very fine particles may be carried with the bleed water to the top resulting in laitance and perhaps the formation of flaws called bleeding channels. In concretes, sedimentation may cause flaws under the larger aggregate particles. If the fresh concrete is not protected from too rapid surface drying, capillary forces cause drying shrinkage that may cause plastic shrinkage cracks. Good construction practices are designed to minimize all of these flaws.

The engineering properties of the concrete, such as strength, elastic moduli, permeability to water and aggressive solutions, and frost resistance, depend strongly on the water–cement ratio and degree of hydration of the cement. A variety of empirical water–cement ratio laws express the strength as functions of water–cement ratio or porosity. The fraction of the original water-filled space, which is occupied by hydration products at any stage of hydration, is termed the gel-space ratio *X*. The compressive strength σ of hardened cement or mortar then approximately fits the power law:

$$\sigma = \sigma_o X^n$$

where *n* is about 3.0 and σ_o is the intrinsic strength of the densest (*X* = 1) gel produced by a given cement under normal hydrating conditions. Values of σ_o range upward from 100 MPa (15,000 psi), depending on the cement composition (44). Several direct relationships between porosity, *p*, and strength have been applied to cement pastes (45–48):

$$\sigma = \sigma_o (1 - p)^B$$
$$\sigma = D \ln (p - p_o)$$
$$\sigma = \sigma_o(1 - Ep)$$

where B, D, and E are constants. Whereas some of these equations break down at very low or very high porosities, they all provide reasonable estimates within an intermediate porosity range. One comparative study concluded that the last equation was the most satisfactory (49). Under extreme conditions, eg, hot pressing at very low water–cement ratios, strengths as high as 655 MPa (95,000 psi) have been reported (50). Tensile strengths and elastic moduli are similarly dependent on porosity or gel-space ratio, but the tensile strength is only about one-tenth the compressive strength. The Young's modulus of the densest gels produced under normal hydrating conditions is ca 34 GPa (5 × 10⁶ psi) (30).

Under sustained loads, hardened cements and concrete creep or deform continuously with time, in addition to the initial elastic deformation. Under normal working loads this deformation may in time exceed the elastic deformation and must be considered in engineering design. This is especially true in prestressed concrete structural members in which steel tendons under high tensile stress maintain compressive stress in the concrete to prevent tensile cracking during bending. Both creep and drying shrinkage of the concrete may lead to loss of prestress. Some creep in ordinary concrete structures and in the cement paste between the aggregate particles can also be an advantage because it tends to reduce stress concentrations, cracking, and microcracking around aggregate particles.

Drying of hardened cements results in shrinkage of the paste structure and of concrete members. Linear shrinkage of hardened cements is about 0.5% when dried to equilibrium at normal (ca 50% rh) relative humidities. The cement gel structure is somewhat stabilized during drying so that upon subsequent wetting and drying smaller changes occur. Concretes shrink much less (about 0.05%), depending on the volume fractions of cement paste and aggregates, water–cement ratio, and other factors. Drying of concrete structural members proceeds very slowly and results in internal shrinkage stresses because of the moisture gradients during drying. Thick sections continue to dry and shrink for many years. Atmospheric carbon dioxide penetrates the partly dried concrete and reacts with the calcium silicate hydrate gel, as well as with calcium aluminate hydrates, releasing additional water and causing additional shrinkage. The density of the hydration products is increased, however, and the strength is actually increased. This reaction is sometimes used to advantage in the manufacture of precast concrete products to improve their ultimate strength and dimensional stability by precarbonation.

The slowness of drying and the penetration of the hardened cement by carbon dioxide or chemically aggressive solutions, eg, seawater or sulfate ground waters, is a result of the small sizes of the pores. Initially the pores in the fresh paste are the water-filled spaces (capillaries) between cement particles. As these spaces become subdivided by the formation of the hydration products, the originally continuous pore system becomes one of more discrete pores or capillary cavities separated from each other by gel formations in which the remaining pores are very much smaller. These gel pores are so small (ca 3 nm nominal diameter) that most of the water contained in them is strongly affected by the solid surface force fields. These force fields are responsible for a large increase in the viscosity of the water and a decrease in mobility of ionic species in solution. Hence, the permeability of the paste to both water and dissolved substances is greatly reduced as hydration proceeds. This in part accounts for the great durability of concrete, especially when water–cement ratios are kept low and adequate moist curing ensures a high degree of hydration. High water–cement ratios result in large numbers of the capillary spaces (0.1 μm and larger) interconnected through capillaries which are 10 nm or larger. These capillaries not only lower the strength, but also permit the easy penetration of aggressive solutions. Furthermore, these capillary spaces may become filled with water which freezes below 0°C, resulting in destructive expansions and deterioration of the concrete.

Chemical Admixtures

Admixtures include materials other than cement, water, or aggregate added immediately before or during mixing. Admixtures serve a broad range of purposes including the control of setting, control of workability, and control of air content.

Retarders and Accelerators. Materials that control hardening of cement may be either organic or inorganic. Retarders are often incorporated in oil well cementing and hot-weather concrete applications, whereas accelerators may be useful for cold-weather concrete applications in which higher rates of reactivity are desirable. In most cases, these admixtures are used in low concentrations, suggesting that they act by adsorption.

Water-Reducing Agents and Superplasticizers. Common admixtures that improve fluidity of concrete mixes are often used in high strength concrete. These admixtures make possible the incorporation of silica fume while maintaining necessary workability. Three principal types of

superplasticizers are in common use: salts of sulfonated melamine formaldehyde polymers; salts of sulfonated naphthalene formaldehyde polymers; and modified lignosulfonate materials (see AMINO RESINS; LIGNIN; PHENOLIC RESINS). One benefit of these admixtures is improved dispersion of cement grains in the mixing water.

Air-Entrainment Agents. Materials that are used to improve the ability of concrete to resist damage from freezing are generally known as air-entrainment agents. These surfactant admixtures (see SURFACTANTS) produce a foam which persists in the mixed concrete, and serves to entrain many small spherical air voids that measure from 10 to 250 μm in diameter. The air voids alleviate internal stresses in the concrete that may occur when the pore solution freezes. In practice, up to 10% air by volume may be entrained in concrete placed in severe environments.

Manufacture

PORTLAND CEMENTS

The process of Portland cement manufacture consists of (1) quarrying and crushing the rock, (2) grinding the carefully proportioned materials to high fineness, (3) subjecting the raw mix to pyroprocessing in a rotary kiln, and (4) grinding the resulting clinker to a fine powder. A layout of a typical plant is shown in Figure 7 (51). Figure 8 gives the layout of a newer dry process plant (52). No new wet process plants are being built, and existing wet process plants are gradually being replaced by dry process plants. The plants outlined are typical of installations producing approximately 1000 metric tons per day. Modern installations (53–55) are equipped with innovations such as suspension or grate preheaters, roller mills, or precalciner installations.

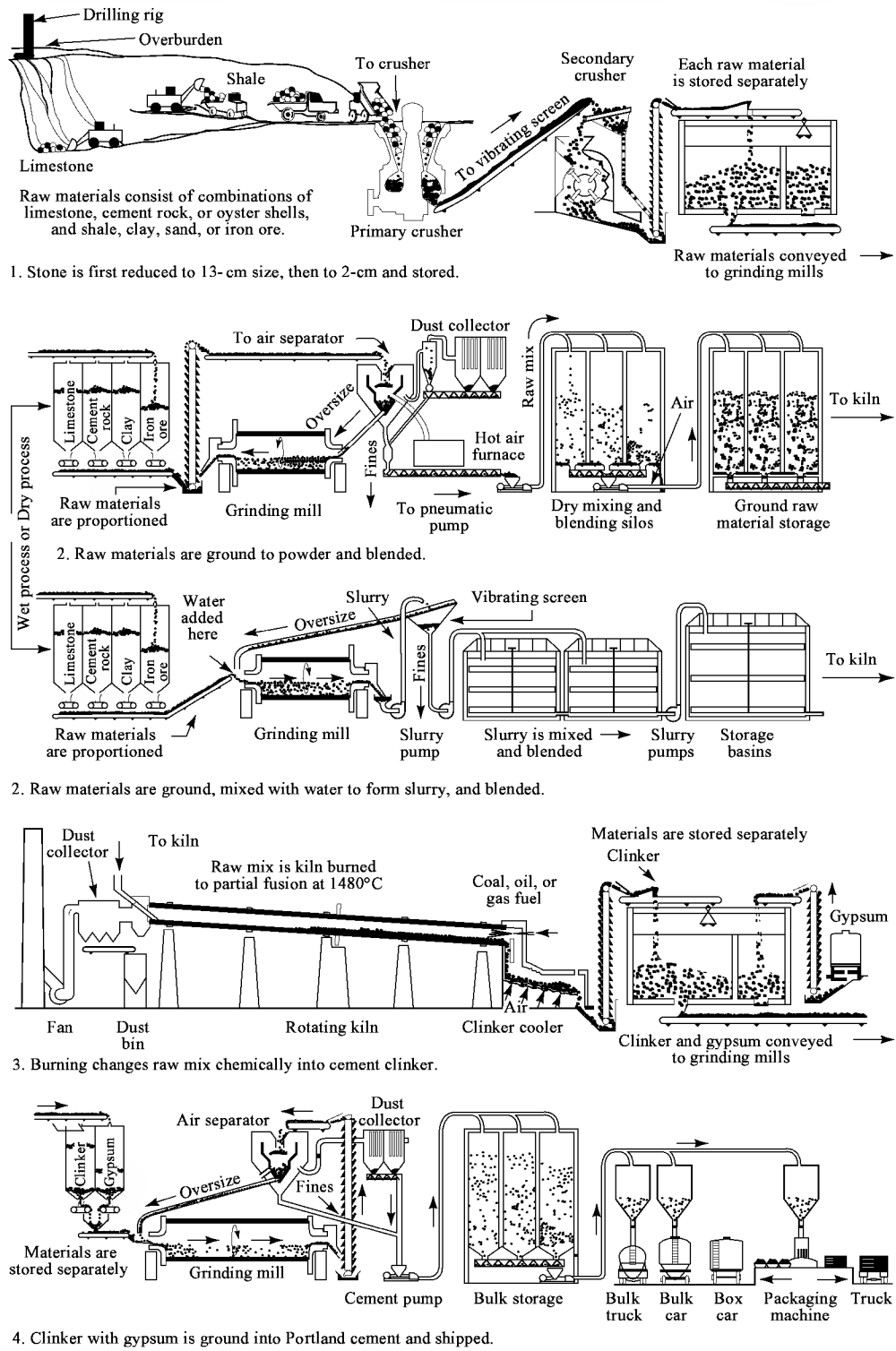
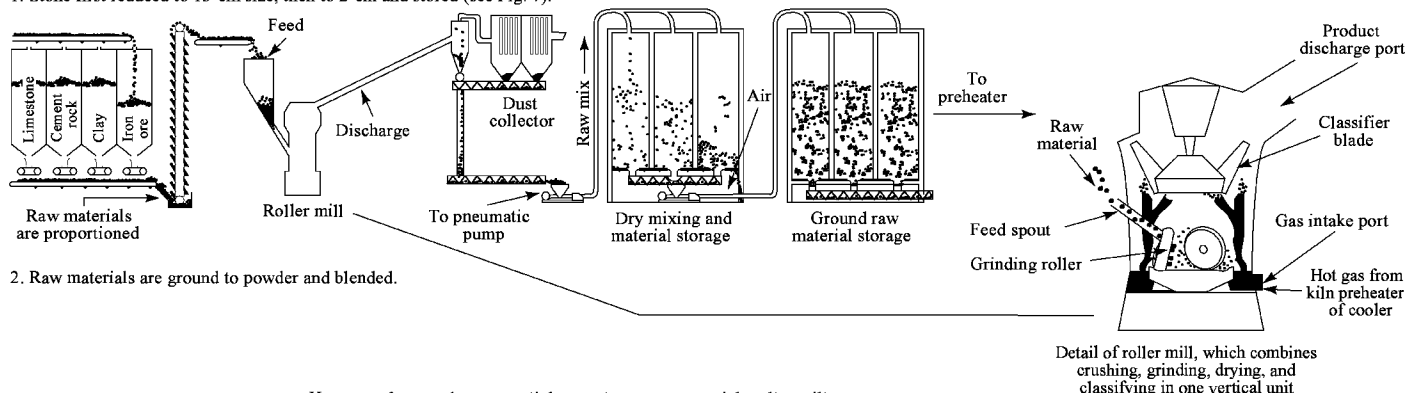


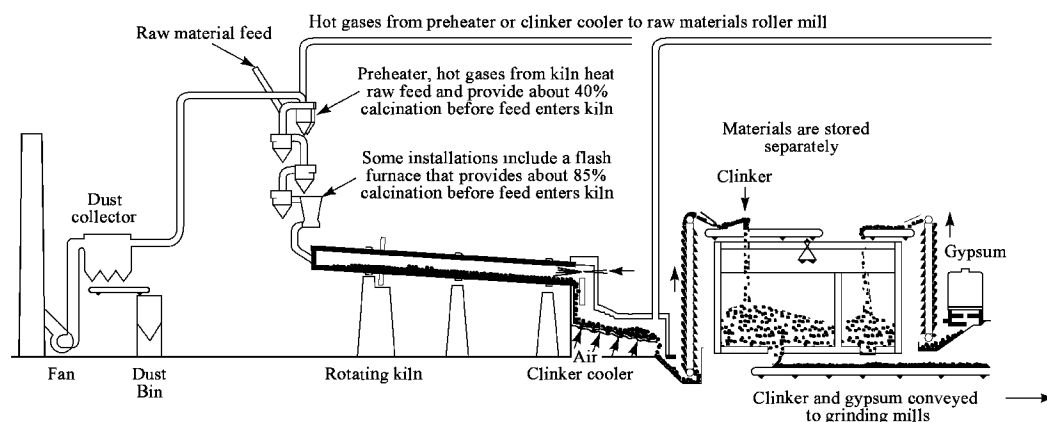
Fig. 7. Steps in the manufacture of Portland cement (51).

Courtesy of Portland Cement Association (51).

1. Stone first reduced to 13-cm size, then to 2-cm and stored (see Fig. 7).



2. Raw materials are ground to powder and blended.



3. Burning changes raw mix chemically into cement clinker. Note four-stage preheater, flash furnaces, and shorter kiln.

4. Clinker with gypsum is ground into Portland cement and shipped (see Fig. 7).

Fig. 8. Technology in dry-process cement manufacture (52).

Courtesy of Portland Cement Association.

Because calcium oxide comprises about 65% of Portland cement, these plants are frequently situated near the source of their calcareous material. The requisite silica and alumina may be derived from a clay, shale, or overburden from a limestone quarry. Such materials usually contain some of the required iron oxide, but many plants need to supplement the iron with mill scale, pyrite cinders, or iron ore. Silica may be supplemented by adding sand to the raw mix, whereas alumina can be furnished by bauxites and Al_2O_3 -rich flint clays.

Industrial by-products are becoming more widely used as raw materials for cement, eg, slags contain carbonate-free lime, as well as substantial levels of silica and alumina. Fly ash from utility boilers can often be a suitable feed component, because it is already finely dispersed and provides silica and alumina. Even vegetable wastes, such as rice hull ash, provide a source of silica. Probably 50% of all industrial by-products are potential raw materials for Portland cement manufacture.

Clinker production requires large quantities of fuel. In the United States, coal (qv) and natural gas are the most widely used kiln fuels but fuels derived from waste materials, eg, tires, solvents, etc, are increasing in importance (53) (see FUELS FROM WASTE; GAS, NATURAL). In addition to the kiln fuel, electrical energy is required to power the equipment. This energy, however, amounts to only about one-ninth that of the kiln fuel. The cement industry carefully considers all measures that can reduce fuel demand.

Raw Materials Preparation. The bulk of the raw material originates in the plant quarry when control of the clinker composition starts with systematic core drillings and selective quarrying. A primary jaw or roll crusher is frequently located within the quarry reducing the quarried limestone or shale to about 100 mm top size. A secondary crusher, usually roll or hammer mills, gives a product of about 10–25 mm top size. Clays may require treatment in a wash mill to separate sand and other high silica material. Combination crusher-dryers utilize exit gases from the kiln or clinker cooler to dry wet material during crushing.

Argillaceous, siliceous, and ferrous raw mix components are added to the crusher product. At the grinding mills, the constituents are fed into the mill separately, using weigh feeders or volumetric measurements. Ball mills are used for wet and dry processes to grind the material to a fineness such that only 15–30 wt % is retained on a 74 μm (200 mesh) sieve. In the wet process the raw materials are ground with about 30–40% water, producing a well-homogenized mixture called slurry. Low concentrations of slurry thinners may be added, such as sodium carbonates, silicates, and phosphates, as well as lignosulfonates and modified petrochemicals. Filter presses or other devices remove water from slurries before feeding into the kiln.

Raw material for dry process plants is ground in closed-circuit ball mills with air separators, which may be set for any desired fineness. Drying is usually carried out in separate units, but waste heat can be utilized directly in the mill by coupling the raw mill to the kiln. Autogenous mills, which operate without grinding media are not widely used. For suspension preheater-type kilns, a roller mill utilizes the exit gas from the preheater to dry the material in suspension in the mill.

A blending system provides the kiln with a homogeneous raw feed. In the wet process the mill slurry is blended in a series of continuously agitated tanks in which the composition, usually the CaO content, is adjusted as required. These tanks may also serve as kiln feed tanks, or the slurry after agitation is pumped to large kiln feed basins. Dry-process blending is usually accomplished in a silo with compressed air.

Pyroprocessing. Nearly all cement clinker is produced in large rotary kiln systems. The rotary kiln is a highly refractory-lined cylindrical steel shell (3–8 m dia, 50–230 m long) equipped with an electrical drive to rotate at 1–3 rpm. It is a countercurrent heating device slightly inclined to the horizontal so that material fed into the upper end travels slowly by gravity to be discharged onto the clinker cooler at the discharge end. The burners at the firing end produce a current of hot gases that heats the clinker and the calcined and raw materials in succession as it passes upward toward the feed end. Highly refractory bricks of magnesia or alumina (see REFRACTORIES) line the firing end, whereas in the less heat-intensive midsection of the kiln bricks of lower refractoriness and thermal conductivity can be used, changing to abrasion-resistant bricks or monolithic castable lining at the feed end. To prevent excessive thermal stresses and chemical reaction of the kiln refractory lining, it is necessary to form a protective coating of clinker minerals on the hot face of the burning zone brick. This coating also reduces kiln shell heat losses by lowering the effective thermal conductivity of the lining.

It is desirable to cool the clinker rapidly as it leaves the burning zone. This is best achieved by using a short, intense flame as close to the discharge as possible. Heat recovery, preheating of combustion air, and fast clinker cooling are achieved by clinker coolers of the traveling-grate, planetary, rotary, or shaft type. Most commonly used are grate coolers where the clinker is conveyed along the grate and subjected to cooling by ambient air, which passes through the clinker bed in crosscurrent heat exchange. The air is moved by a series of undergrate fans, and becomes preheated to 370–800°C at the hot end of the cooler. It then serves as secondary combustion air in the kiln; the primary air is that portion of the combustion air needed to carry the fuel into

the kiln and disperse the fuel.

During the burning process, the high temperatures cause vaporization of alkalis, sulfur, and halides. These materials are carried by the combustion gases into the cooler portions of the kiln system where they condense, or they may be carried out to the kiln dust collector, usually a fabric filter or electrostatic precipitator, together with partially calcined feed and unprocessed raw feed. This kiln dust is reusable. However, ASTM specifications limit the total SO₃ content of the finished cement to 2.3–4.5%, depending on the cement type and C₃A content. Similarly, an optional ASTM C150 specifications limits the total alkali content of the cement to 0.60%, expressed as equivalent Na₂O. Other potential and actual uses of dust include fertilizer supplements (see FERTILIZERS), acid mine waste neutralization (see WASTES, INDUSTRIAL), boiler SO₂ control, and soil stabilization (qv).

Wet-Process Kilns. In a long wet-process kiln, the slurry introduced into the feed end first undergoes simultaneous heating and drying. The refractory lining is alternately heated by the gases when exposed and cooled by the slurry when immersed; thus the lining serves to transfer heat, as do the gases themselves. Large quantities of water must be evaporated, thus most wet kilns are equipped with chains to maximize heat transfer from the gases to the slurry. Large, dense chain systems permit energy savings of up to 1.7 MJ/kg (731 Btu/lb) clinker in exceptionally favorable situations (53). After most of the moisture has been evaporated, nodules, which still contain combined water, move down the kiln and are gradually heated to about 550°C. As the charge leaves the burning zone it begins to cool, and tricalcium aluminate and magnesia crystallize from the melt and the liquid phase finally solidifies to produce the ferrite phase. The material drops into the clinker cooler for further cooling by air.

Dry-Process Kilns, Suspension Preheaters, and Precalciners. The dry process for cement manufacture utilizes a dry kiln feed rather than a slurry. Early dry-process kilns were short, and the substantial quantities of waste heat in the exit gases from such kilns were frequently used in boilers for electric power generation (qv); the power generated was frequently sufficient for all electrical needs of the plant. In one modification, the kiln has been lengthened and chains have been added; however, these serve almost exclusively a heat-exchange function (see HEAT EXCHANGE TECHNOLOGY). Refractory heat-recuperative devices, such as crosses, lifters, and trefoils, have also been installed so that the long dry kiln is energy efficient. Other than the need for evaporation of water, its operation is similar to that of a long wet kiln.

A second type of modern dry-process kiln is the suspension preheater system (56). The dry, pulverized feed passes through a series of cyclones where it is separated and preheated several times. The partially calcined feed exits the preheater tower into the kiln at about 800–900°C. The kiln length required for completion of the process is considerably shorter than that of conventional kilns, and heat exchange is very good. Suspension preheater kilns are very energy-efficient: as low as 3.1 MJ/kg (1334 Btu/lb) clinker in large installations. The intimate mixing of the hot gases and feed in the preheaters promotes condensation of alkalis and sulfur on the feed, sometimes resulting in objectionably high alkali and sulfur contents in the clinker. To alleviate this problem, some of the kiln exit gases can be bypassed and fewer cyclone stages used in the preheater with some sacrifice of efficiency.

The success of preheater kiln systems led to precalciner kiln systems. These units utilize a second burner to carry out calcination in a separate vessel attached to the preheater. The flash furnace (57), eg, utilizes preheated combustion air drawn from the clinker cooler and kiln exit gases and is equipped with an oil burner that burns about 60% of the total kiln fuel. The raw material is calcined almost 95%, and the gases continue their upward movement through successive preheater stages in the same manner as in an ordinary preheater.

The precalciner system permits the use of smaller kilns because only actual clinkering is carried out in the rotary kiln. Energy efficiency is comparable to that of a preheater kiln, except that the energy penalty for bypass of kiln exit gases is reduced because only about 40% of the fuel is being burned in the kiln. Precalciner kilns in operation in Japan produce up to 10,000 metric tons of clinker per day; the largest long wet-process kiln, in Clarksville, Missouri, produces only 3270 t/d by comparison. The burning process and clinker cooling operations for the modern dry-process kiln systems are the same as for long wet kilns.

Finish Grinding. The cooled clinker is conveyed to clinker storage or mixed with 4–6% gypsum and introduced directly into the finish mills. The clinker and gypsum are ground to a fine, homogeneous powder having a surface area of about 3000–5000 cm²/g. About 85–96% of the product is in particles having 44 μm dia. These objectives may be accomplished by two different mill systems. In open-circuit milling, the material passes directly through the mill without any separation. A wide particle size distribution range is usually obtained with substantial amounts of very fine and rather coarse particles. In closed-circuit grinding the mill product is carried to a cyclonic air separator in which the coarse particles are rejected from the product and returned to the mill for further grinding. Energy requirements for finish grinding vary from about 33–77 kWh/t cement, depending also on the nature of the clinker.

Computer Control. Process computer control was introduced to the cement industry in the 1960s and a plant of a capacity of 1 million metric tons per year was built and placed in operation in 1973 having complete computer process and segmental control (58). Other plants have been built and some older plants computerized (59). Variables can be measured at intervals of 0.25 s and overall optimum response to operating problems is programmed, not always possible with manual operation. The rotary kiln is the largest and most difficult equipment to operate. Temperature-sensing and gas-analyzing devices present problems.

Quality Control. Beginning at the quarry operation, product quality is maintained by adjustments of composition, burning conditions, and finish grinding. Control checks are made for fineness of materials, chemical composition, and uniformity. Clinker burning is monitored by weighing a portion of sized clinker, known as the liter weight test, a free lime test, or checked by microscopic evaluation of the crystalline structure of the clinker compounds. Samples may be analyzed by x-ray fluorescence, atomic absorption, and flame photometry (see SPECTROSCOPY). Wet chemistry is described in ASTM C114 (24). Standard cement samples are available from the National Institute of Standards and Technology. Fineness of the cement is most commonly measured by the air permeability method. Finally, standardized performance tests are conducted on the finished cement (24).

Environmental Pollution Control. The cement industry has had an intensive program of capital expenditure to install dust collection equipment on kilns and coolers since the 1970s (60). Modern equipment collects dust at 99.8% efficiency. Many smaller dust collectors are installed in new plants (61).

The Federal Water Pollution Control Act Amendments of 1972 (62) established limits for cement plant effluents including water run-off from manufacturing facilities, quarrying, raw material storage piles, and wastewater. Compliance with these standards has required construction of diversion ditches for surface water, ponds for settling and clarification, dikes and containment structures for possible oil spills, and chemical water treatment in some cases. Since the cement industry obtains most of its raw material by quarrying, the standards for the mineral industry also apply.

One of the primary waste products of cement manufacturing is cement kiln dust (CKD). CKD is collected from exhaust gases and either returned to the kiln with other raw materials or disposed of as landfill. CKD is also used in other applications, such as synthetic aggregate. CKD tends to accumulate very low concentrations of heavy metals that originate in the fuels or in the raw materials. These metals volatilize in the high temperatures of the kiln and become associated with exhaust gases. Two significant studies of CKD (63,64) concluded that the environmental considerations are minor and that neither CKD nor cement have characteristics of hazardous waste as defined under the *Resource Conservation and Recovery Act*. The cement industry continues to search for new uses for CKD in construction applications.

SPECIAL PURPOSE AND BLENDED CEMENTS

Special purpose and blended Portland cements are manufactured essentially by the same processes as ordinary Portland cements but have specific compositional and process differences. White cements are made from raw materials of very low iron content. This type is often difficult to burn because almost the entire liquid phase must be furnished by calcium aluminates. As a consequence of the generally lower total liquid-phase content, high burning-zone temperatures may be necessary. Fast cooling and occasionally oil sprays are needed to maintain both quality and color.

Regulated set cements are made using fluorite, CaF₂, additions which also act as fluxing agents, or mineralizers, to reduce burning temperatures. The clinker produced then contains C₁₁A₇·CaF₂, (mixed notation) as a principal phase. Another regulated set cement can be made in which the principal constituents are C₄A₃Š and belite. Both cements rapidly harden and can reach modest compressive strengths within several hours. Final material properties are in most respects similar to comparable concretes made with Portland cement.

Concern with regard to energy conservation has prompted the use of byproduct materials in Portland cement concrete. Blended hydraulic cements are produced by intimately and uniformly blending two or more types of fine materials. The primary blending materials are Portland cement, ground

granulated blast-furnace slag, fly ash and other pozzolans, hydrated lime, and preblended cement combinations of these materials. Cement kiln dust and other materials are undergoing research for use in blended cements. Blended hydraulic cements must conform to the requirements of ASTM C595, which recognizes five classes of blended cements: Portland blast-furnace slag cement, Type IS; Portland-pozzolan cement, Type IP and Type P; slag cement, Type S; pozzolan-modified Portland cement, Type I (PM); and slag-modified Portland cement, Type I (SM).

Blended cements represent about 1% of the cement shipped in the United States. In Europe, the use of blended cement is very common. Most of the blended cement used in the United States is Type IP and it is used in the same applications as that of regular Type I or II Portland cement.

ASTM C845 Type E-I (K) expansive cement manufactured in the United States usually depends on aluminate and sulfate phases that result in more ettringite formation during hydration than in normal Portland cements. Type K contains an anhydrous calcium sulfoaluminate, C₄A₃S̄. This cement can be made either by integrally burning to produce the desired phase composition, or by intergrinding a special component with ordinary Portland cement clinkers and calcium sulfate.

Oil well cements are manufactured similarly to ordinary Portland cements except that the goal is usually sluggish reactivity. For this reason, levels of C₃A, C₃S, and alkali sulfates are kept low. Hydration-retarding additives are also employed.

Pozzolans include natural materials such as diatomaceous earths (see DIATOMITE), opaline cherts, and shales, tuffs, and volcanic ashes or pumicites, and calcined materials such as some clays and shales. By-products such as fly ashes and silica fume are also employed. In the United States the proportion of pozzolan interground with clinker has varied from 15 to over 30%, whereas in Italy, cements with a 30–40% pozzolan content are produced.

In some European countries Portland cement clinker is interground with 10–65% granulated blast-furnace slag to produce a Portland blast-furnace slag cement. The composition of the slag varies considerably but usually falls within the following wt % composition ranges: CaO, 40–50%, SiO₂, 30–40%, Al₂O₃, 8–18%; MgO, 0–8%; S (sulfide), 0–2%; and FeO, MnO, 0–3%.

Most masonry cements are finely interground mixtures where Portland cement is a principal constituent. These cements also include finely ground limestones, hydrated lime, natural cement, pozzolans, clays, or air-entraining agents. Secondary materials are used to impart the required water retention and plasticity to mortars.

NONPORTLAND CEMENTS

Calcium Aluminate Cements. These cements are manufactured by heating until molten or by sintering a mixture of limestone and bauxite with small amounts of SiO₂, FeO, and TiO₂ (see ALUMINUM COMPOUNDS, ALUMINUM OXIDE, CALCINED, TABULAR, AND ALUMINATE CEMENTS). In Europe the process is usually carried out in an open-hearth furnace having a long vertical stack into which the mixture of raw materials is charged. The hot gases produced by a blast of pulverized coal and air pass through the charge and carry off the water and carbon dioxide. Fusion occurs when the charge drops from the vertical stack onto the hearth at about 1425–1500°C. The molten liquid runs out continuously into steel pans on an endless belt in which the melt solidifies. Special rotary kilns, provided with a tap hole from which the molten liquid is drawn intermittently, and electric arc furnaces have also been used.

When calcium aluminate cements are made by the fusion process, the solidified melt must be crushed and then ground. The material is very hard to grind and power consumption is high.

Supersulfated Cement. Supersulfated cement contains about 80% slag interground with 15% gypsum or anhydrite and 5% Portland cement clinker. The main hydration products are C–S–H and ettringite. More water is taken up during curing than with Portland or normal slag cements and the content of nonevaporable water is higher.

Hydraulic Limes. These materials are produced by heating below sintering temperature a limestone containing considerable clay, during which some combination takes place between the lime and the oxides of the clay to form hydraulic compounds.

Economic Aspects and Environmental Issues

From the beginning of the United States Portland cement industry in 1872, annual cement consumption grew through 1970. From 1975 to 1990, cement consumption has been little changed. Annual production and sales tonnages are nearly identical; Table 8 gives United States' production figures and Table 9 the world production. China, having an annual output of about 200 million metric tons in 1990, has emerged as the world's leading cement producer (68).

Table 8. United States Portland Cement Production^a

Year	Production, 100 metric tons	Number of plants	Average production per plant, 1000 metric tons
1970	66,378	181	367
1975	60,597	164	511
1980	68,243	151	452
1990	69,940	119	587

^a Refs. 65, 66.

Table 9. World Portland Cement Production^a, 10⁶t

Region	1970	1980	1989
Europe	322	383	421
France	29	31	27
Germany	37	33	27
Italy	33	42	41
USSR	95	125	140
Spain	16	30	28
United Kingdom	18	15	18
Africa	18	32	52
North America	111	154	166
United States	69	68	70
Canada	7	10	12
Asia	132	277	491
Japan	57	87	79
Oceania	6	7	8
<i>World Total</i>	<i>590</i>	<i>881</i>	<i>1138</i>

^a Ref. 67.

Since World War II, the cement industry reduced labor and energy costs by increased investment in capital equipment and larger plants to remain

competitive with other building materials industries (see BUILDING MATERIALS, SURVEY; BUILDING MATERIALS, PLASTIC). The average plant size more than doubled between 1950 and 1990.

Energy Usage. Over a 40-year span the cement industry has reduced unit energy usage by 40% , from 9.6 MJ /kg (4131 Btu /lb) in 1950 to 5.7 MJ /kg (2464 Btu /lb) in 1990. The wet process, used in 60% of the plants in the 1960s, is less labor-intensive than the dry process. However, as energy costs escalated in the early 1970s, the more energy efficient dry-process manufacturing was preferred. According to 1989 figures, wet-process plants consume 38% more energy per ton of cement than dry-process plants.

Coal was the primary kiln fuel in 1989 as seen in Table 10. Energy from coal rose from 39 to 84% of the total energy required for cement production between 1972 and 1989. In the same time period, natural gas dropped to 9% , petroleum products to 1% of the total energy consumed. Waste fuels represented 5% of the energy consumed in 1989 cement production.

Table 10. United States Portland Cement Industry Energy Consumption ^a , %

Fuel	Distribution ^a Year	
	1972	1989
coal and coke	38.6	84.2
natural gas	48.3	9.3
petroleum products	13.1	1.3
waste fuel	0.0	5.2
<i>Total fossil fuel</i>	<i>100.0</i>	<i>100.0</i>
fossil fuel	93.4	89.7
electricity	6.6	10.3
<i>Total fuel and power</i>	<i>100.0</i>	<i>100.0</i>

^a Ref. 69.

Marketing Patterns. The cement industry has reduced its dependence on bag (container) shipments (54.7% in 1950) and turned to the more labor-efficient bulk transport (96% in 1990). In addition, the amount of cement shipped by rail transportation declined from 75% of industry shipments in 1950 to less than 14% in 1990. Table 11 summarizes the shipment distribution by cement type.

Table 11. United States Portland Cement Shipments by Type ^{a,b} , 1990

Type	Shipments, 10 ³ t	Average value, \$ /t
Types I and II	77,342	48.60
Type III	3,152	50.55
oil well	963	45.97
white	415	156.40
Type V	957	58.45
Portland slag and pozzolan	436	54.30
expansive	45	98.48
miscellaneous	1,060	59.19
<i>Total</i>	<i>84,370</i>	<i>49.47</i>

^a Ref. 65.

^b See Tables 4 and 5.

In the past 30 years, the ready-mixed concrete industry became the primary customer for cement manufacturers. In 1990 more than 72% of the cement shipped was sold to the ready-mixed concrete industry, compared with 63% in 1975. The other primary uses are in building materials, concrete products, and highway construction.

Environmental Aspects

Cement plants in the United States are now carefully monitored for compliance with Environmental Protection Agency (EPA) standards for emissions of particulates, SO₂, NO_x, and hydrocarbons. All plants incorporate particulate collection devices such as baghouses and electrostatic precipitators (see AIR POLLUTION CONTROL METHODS). The particulates removed from stack emissions are called cement kiln dust (CKD). It has been shown that CKD is characterized by low concentrations of metals which leach from the CKD at levels far below regulatory limits (63,64). Environmental issues continue to be of concern as the use of waste fuel in cement kilns becomes more widespread.

Specifications and Types

Portland cements are manufactured to comply with specifications established in each country (70). In the United States, several different specifications are used, including those of the American Society for Testing and Materials and American Association of State Highway and Transportation Officials (AASHTO). The ASTM annually publishes test methods and standards (24), which are established on a consensus basis by its members which include consumers and producers.

In the United States, Portland cement is classified in five general types designated by ASTM Specification C150 (24): Type I, when the special properties are not required; Type II, for general use, and especially when moderate sulfate resistance or moderate heat of hydration is desired; Type III, for high early strength; Type IV, for low heat of hydration; and Type V, for high sulfate resistance. Types I, II, and III may also be specified as air-entraining. Chemical compositional, physical, and performance test requirements are specified for each type; optional requirements for particular uses may also be specified.

Other countries have similar types, some classifications, as in Germany, are based on age-strength levels by standard tests (70). A product made in Italy and France known as Ferrari cement is similar to Type V and is sulfate-resistant. Such cements have high iron oxide and low alumina contents, and harden more slowly.

Uses

Hydraulic cements are intermediate products used for making concretes, mortars, grouts, asbestos–cement products, and other composite materials (qv). High early strength cements may be required for precast concrete products or in high-rise building frames to permit rapid removal of forms and early load carrying capacity. Cements of low heat of hydration may be required for use in massive structures, such as gravity dams, to prevent excessive temperature rise and thermal contraction and cracking during subsequent cooling. Concretes exposed to seawater or sulfate-containing ground waters require cements that are sulfate-resistant after hardening.

Air-entraining cements produce concretes that protect the concrete from frost damage. They are commonly used for concrete pavements subjected to wet and freezing conditions. Cement of low alkali content may be used with certain concrete aggregates containing reactive silica to prevent deleterious expansions.

Expansive, or shrinkage-compensating cements cause slight expansion of the concrete during hardening. The expansion has to be elastically restrained so that compressive stress develops in the concrete (71). Subsequent drying and shrinkage reduces the compressive stresses but does not result in tensile stresses large enough to cause cracks. Special highly expansive cements have been used for demolition purposes.

Finely ground cements, often called ultrafine cements, having particles less than 10 µm and an average size of 4 µm are used to grout soils with fine pore spaces, such as fine sand with a permeability of 10⁻⁴ cm s. These cements can be made with a wide combination of Portland cement, slag, or silica fume (72).

Regulated-set cement, called jet cement in Japan, is formulated to yield a controlled short setting time, <1 h, and very early strength (73). It is a modified cement that can be manufactured in a conventional Portland cement kiln. It incorporates set control and early strength development components.

Natural cements (74) which may be regarded as intermediate between Portland cements and hydraulic limes in hydraulic activity, are no longer available in the United States.

Blended cements. Portland cement clinker is also interground with suitable other materials such as granulated blast-furnace slags and natural or artificial pozzolans. These substances also show hydraulic activity when used with cements, and the blended cements (75) bear special designations such as Portland blast-furnace slag cement or Portland–pozzolan cement. Pozzolans are used in making concrete both as an interground component of the cement and as a direct addition to the concrete mix. It is only when the two materials are interground that the mixture can be referred to as Portland–pozzolan cement. Portland–pozzolan cements (76) were developed originally to provide concretes of improved economy and durability in marine, hydraulic, and underground environments; they also prevent deleterious alkali–aggregate reactions. Blast-furnace slag cements (77) also reduce deleterious alkali–aggregate reactions and can be resistant to seawater if the slag and cement compositions are suitably restricted. Both cements hydrate and harden more slowly than Portland cement. This can be an advantage in mass concrete structures where the lower rates of heat liberation may prevent excessive temperature rise, but when used at low temperatures the rate of hardening may be excessively slow. Portland blast-furnace slag cements may be used to advantage in steam-cured products which can have strengths as high as obtained with Portland cement. Interest in the use of blended cements is stimulated by energy conservation and solid waste utilization considerations.

Oil well cements (78) are usually made from Portland cement clinker and may also be blended cements. The American Petroleum Institute Specification for Materials and Testing for Well Cements (*API Specification 10*) (78) includes requirements for nine classes of oil well cements. They are specially produced for cementing the steel casing of gas and oil wells to the walls of the bore-hole and to seal porous formations (79). Under these high temperature and pressure conditions ordinary Portland cements would not flow properly and would set prematurely. Oil well cements are more coarsely ground than normal, and contain special retarding admixtures.

Masonry cements (80) are cements for use in mortars for masonry construction. They are formulated to yield easily workable mortars and contain special additives that reduce the loss of water from the mortar to the porous masonry units.

Calcium aluminate cement (81) develops very high strengths at early ages. It attains nearly its maximum strength in one day, which is much higher than the strength developed by Portland cement in that time. At higher temperatures, however, the strength drops off rapidly. Heat is also evolved rapidly on hydration and results in high temperatures; long exposures under moist warm conditions can lead to failure. Resistance to corrosion in sea or sulfate waters, as well as to weak solutions of mineral acids, is outstanding. This cement is attacked rapidly, however, by alkali carbonates. An important use of high alumina cement is in refractory concrete for withstanding temperatures up to 1500°C. White calcium aluminate cements, with a fused aggregate of pure alumina, withstand temperatures up to 1800°C.

Supersulfated cement (82) has a very low heat of hydration and low drying shrinkage. It has been used in Europe for mass concrete construction and especially for structures exposed to sulfate and seawaters.

Tief cements (83), manufactured in Belgium, are produced as a wet slurry of finely ground slag. When activators such as Portland cement, lime, or sodium hydroxide are added in a concrete mixer, the slurry sets and hardens to produce concretes with good strength and durability.

Hydraulic limes (84) may be used for mortar, stucco, or the scratch coat for plaster. They harden slowly under water, whereas high calcium limes, after slaking with water, harden in air to form the carbonate but not under water at ordinary temperatures. However, at elevated temperatures achieved with steam curing, lime–silica sand mixtures do react to produce durable products such as sand–lime bricks.

Specialty cements. For special architectural applications, white Portland cement with a very low iron oxide content can be produced. Colored cements are usually prepared by intergrinding 5–10% of pigment with white cement.

Numerous other specialty cements composed of various magnesium, barium, and strontium compounds as silicates, aluminates, and phosphates, as well as others, are also produced (85).

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CENTRAL NERVOUS SYSTEM AGENTS.

See NEUROREGULATORS; PSYCHOPHARMACOLOGICAL AGENTS; OPIOIDS, ENDOGENOUS.

CEPHALOSPORINS.

See ANTIBIOTICS, β -LACTAMS.

CERAMIC COLORS.

See COLORANTS FOR CERAMICS.

CERAMIC FIBERS.

See REFRACTORY FIBERS.

CERAMICS

Overview,
Ceramic processing,
Mechanical properties and behavior,
Glass structure and properties,
Nonlinear optical and electrooptic ceramics,
Electronic properties and material structure,

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OVERVIEW

Ceramics may be defined as a class of inorganic, nonmetallic solids that are subjected to high temperature in manufacture or use. Ceramics are distinguished both from metals and metallic alloys and from organic materials such as polymers and plastics, and although syntheses may involve solutions or colloids, the final products are solids. The most common ceramics are oxides, carbides (qv), and nitrides (qv), but silicides, borides, phosphides, sulfides, tellurides, and selenides are ceramics, as well as elemental materials such as carbon (qv) and silicon (see SILICON AND SILICON ALLOYS). Ceramic synthesis and processing generally involve high temperatures and the resulting materials are refractory or heat resistant (see RREFRACTORIES). Ceramics are commonly thought to include only polycrystalline materials, but glasses, which are noncrystalline, and single-crystal materials such as ruby lasers, are classified as ceramics (see GLASS; LASERS). Examples of applications of less common ceramics include quartz optical fibers (see FIBER OPTICS) that are revolutionizing telecommunications, the insulating tiles on the space shuttle (see ABLATIVE MATERIALS), silicon nitride turbocharger rotors used in some passenger automobiles, and the cordierite multilayer substrates used as chip carriers in the latest generation of supercomputers (see COMPUTER TECHNOLOGY).

Ceramic components are frequently made by sintering of powders. Alternatives such as melt processing are often uneconomical because many ceramics have very high melting temperatures or decompose before melting. Many ceramic melts are also very reactive with container materials, which imposes additional limitations on available processing methods. A rule of thumb in ceramic processing is that the quality of a ceramic part is no better than the quality of the powder from which it is made. Thus, much effort has been directed to improving the properties of ceramic powders. Improvements include higher purity, finer particle size, less agglomeration, and better control of compositions and distributions of dopants.

One of the many possible ways of classifying ceramics is according to use. One group is the bulk or commodity ceramics that have had relatively little processing beyond the constituent raw materials. These are primarily low value-added materials such as brick, tile, pottery, and abrasive grain (see ABRASIVES). At the other extreme are the engineering or fine ceramics that are characterized as low volume, high value-added, highly processed materials having carefully controlled properties (see ADVANCED CERAMICS). Some of the main types of engineering ceramics include: (1) electronic ceramics, which include dielectrics, ferroelectrics (qv), ferromagnetic ceramics, piezoelectrics, and superconductors (see also CERAMICS AS ELECTRICAL MATERIALS); (2) structural ceramics, which are strong, fracture-resistant materials such as silicon nitride [12033-89-5], Si₃N₄, silicon carbide [409-21-2], SiC, and toughened zirconium dioxide [1314-23-4], ZrO₂; (3) wear-resistant ceramics, such as the carbides, nitrides, and borides (see BORON COMPOUNDS; TOOL MATERIALS); (4) optical ceramics such as Cr doped Al₂O₃ (ruby [12174-49-1]); silicon dioxide [7631-86-9], SiO₂, fiber; lead lanthanum zirconium titanate (PLZT); and yttrium aluminum garnet (YAG); and (5) bioceramics, which are low or controlled reactivity materials for in-body use such as aluminum oxide [1344-28-1], Al₂O₃, and hydroxyapatite [1306-06-5] (see PROSTHETIC AND BIOMEDICAL DEVICES).

Some of the many ceramic materials and precursors discussed in the following sections are listed in Table 1.

Table 1. Ceramics and Precursors Discussed in Text

Material	CAS Registry Number	Molecular formula
acetic acid	[64-19-7]	CH ₃ COOH
aluminum	[7429-90-5]	Al
aluminum nitride	[24304-00-5]	AlN
aluminum oxide	[1344-28-1]	Al ₂ O ₃
aluminum silicate	[12141-46-7]	3Al ₂ O ₃ ·2SiO ₂
ammonium hydroxide	[1336-21-6]	NH ₄ OH
antimony oxide	[1314-60-9]	Sb ₂ O ₃
arsenic(III) oxide	[1327-53-3]	As ₂ O ₃
arsenic(V) oxide	[1303-28-2]	As ₂ O ₅
barium titanate	[12047-27-7]	BaTiO ₃
beryllia	[1304-56-9]	BeO
beryllium oxide	[1304-56-9]	BeO
bismuth calcium strontium copper oxide		Bi ₂ CaSr ₂ Cu ₂ O _x
bismuth(III) oxide	[1304-76-3]	Bi ₂ O ₃
boron nitride (cubic)	[10043-11-5]	BN
boron phosphide (cubic)	[12777-46-7]	BP
boron trioxide	[1303-86-2]	B ₂ O ₃
calcium oxide	[1305-78-8]	CaO
carbon	[14762-74-4]	C
carbon dioxide	[124-38-9]	CO ₂
carbonic acid	[463-79-6]	H ₂ CO ₄
chromium dioxide	[12018-01-8]	CrO ₂
cobalt ferrite	[12052-28-7]	CoFe ₂ O ₄
copper	[7440-50-8]	Cu
cordierite	[1302-88-1]	2MgO·2Al ₂ O ₃ ·5SiO ₂
cuprous oxide	[1317-39-1]	Cu ₂ O
diamond	[7782-40-3]	C
diethanolamine	[111-42-2]	(HOCH ₂ CH ₂) ₂ NH
feldspar	[68476-25-5]	(K,Na) ₂ O·Al ₂ O ₃ ·6SiO ₂
ferric oxide	[1309-37-1]	Fe ₂ O ₃
ferrite	[1317-54-0]	(Mn _{1-x} Mg _x)Fe ₂ O ₄ (M _{1-x} Zn _x)Fe ₂ O ₄ M = divalent ion
ferrosoferric oxide	[1317-61-9]	Fe ₃ O ₄
flint (fused silica)	[60676-86-0]	SiO ₂
gadolinium garnet		Gd ₂ O ₃ ·5Fe ₂ O ₃

gallium arsenide	[1303-00-0]	GaAs
gallium aluminum nitride	[39460-99-6]	GaAlN
gallium nitride	[25617-97-4]	GaN
gallium oxide	[12024-21-4]	Ga ₂ O ₃
germanium dioxide	[1310-53-8]	GeO ₂
graphite	[7782-42-5]	C
indium oxide	[1312-43-2]	In ₂ O ₃
indium phosphide	[22398-80-7]	InP
iron	[7439-89-6]	Fe
2-propanol	[67-63-0]	(CH ₃) ₂ CHOH
kaolin	[1332-58-7]	
lanthanum barium copper oxide		LaBaCuO ₄
lanthanum oxide	[7439-91-0]	La ₂ O ₃
lead	[7439-92-1]	Pb
lead acetate trihydrate	[6080-56-4]	Pb(OOCCH ₃) ₂ ·3H ₂ O
lead lanthanum zirconate titanate		Pb _{1-x} La (Zr _{1-x} Ti _x)O ₃
lead magnesium niobate (PMN)		Pb(Mg ₁₋₃ Nb ₂₋₃)O ₃
lead monoxide	[1317-36-8]	PbO
lead oxide	[1317-36-8]	PbO
lead titanate	[12060-00-3]	PbTiO ₃
lead zirconate	[12060-01-4]	PbZrO ₃
lead zinc niobate (PZN)		Pb(Zn ₁₋₃ Nb ₂₋₃)O ₃
lead zirconate titanate		Pb(Zr,Ti)O ₃
lithium niobate	[12031-63-9]	LiNbO ₃
lithium tantalate	[12031-66-2]	LiTaO ₃
magnesium oxide	[1309-48-4]	MgO
manganese ferrite	[12063-10-4]	MnFe ₂ O ₄
methanol	[67-56-1]	CH ₃ OH
methoxyethanol	[109-86-4]	CH ₃ OCH ₂ CH ₂ OH
molybdenum disulfide	[1317-33-5]	MoS ₂
molybdenum(VI) oxide	[1313-27-5]	MoO ₃
mullite	[1302-93-8]	3Al ₂ O ₃ ·2SiO ₂
neodymium oxide	[7440-65-5]	Nd ₂ O ₃
nickel ferrite	[12168-54-6]	NiFe ₂ O ₄
nickel monoxide	[1313-99-1]	NiO
niobium(V) oxide	[1313-96-8]	Nb ₂ O ₅
nylon-6	[25038-54-4]	[-NH(CH ₂) NHCO(CH ₂) ₄ CO-] _n
oxalic acid	[144-62-7]	H ₂ C ₂ O ₄
2,4-pentadione	[123-54-6]	CH ₃ COCH ₂ COCH ₃
phosphorous pentoxide	[1314-56-3]	P ₂ O ₅
potassium niobate	[12030-85-2]	KNbO ₃
rhenum trioxide	[1314-28-9]	ReO ₃
silica	[10097-28-6]	SiO ₂
silicon	[7440-21-3]	Si
silicon carbide	[409-21-2]	SiC
silicon nitride	[12033-89-5]	Si ₃ N ₄
sodium chloride	[7647-14-5]	NaCl
spinel	[1302-67-6]	MgAl ₂ O ₄
stannic dioxide	[18282-10-5]	SnO ₂
strontium hexaferrite		SrO·6Fe ₂ O ₃
strontium oxide	[1314-11-0]	SrO
strontium titanate	[12060-59-2]	SrTiO ₃
tantalum(V) oxide	[1314-61-0]	Ta ₂ O ₅
tellurium(IV) oxide	[7446-07-3]	TeO ₂
thallium calcium barium copper oxide		Tl ₂ Ca ₂ Ba ₂ Cu ₃ O ₇
titania	[13463-67-7]	TiO ₂
titanium dioxide	[13463-67-7]	TiO ₂
titanium isopropoxide	[546-68-9]	Ti(OC ₃ H ₇) ₄
titanium(IV) oxide	[1317-80-2]	TiO ₂
triaxial porcelain		Al ₂ O ₃ ·(K,Na) ₂ O·SiO ₂
triethanolamine	[102-71-6]	(HOCH ₂ CH ₂) ₃ N
tungsten(VI) oxide	[1314-35-8]	WO ₃
vanadium(V) oxide	[1314-62-1]	V ₂ O ₅
yttria	[1314-36-9]	Y ₂ O ₃
yttrium barium copper oxide	[107539-20-8]	YBa ₂ Cu ₃ O _{7-δ}
yttrium iron oxide	[12063-56-8]	Y ₂ O ₃ ·Fe ₂ O ₃
yttrium oxide	[7440-65-5]	Y ₂ O ₃
yttrium garnet		Y ₂ O ₃ ·5Fe ₂ O ₃
zinc ferrite	[12063-19-3]	ZnFe ₂ O ₄
zinc oxide	[1314-13-2]	ZnO
zirconia	[1314-23-4]	ZrO ₂
zirconium oxide	[1314-23-4]	ZrO ₂

zirconium *n*-propoxide

[23519-77-9]

Zr(OC₃H₇)₄

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CERAMIC PROCESSING

Processing is key to the reproducible manufacture of ceramics. The tolerance of a finished ceramic to defects determines the raw materials selected, and the control that must be exercised during processing. More expensive advanced ceramics require higher quality, more expensive raw materials coupled with more carefully controlled manufacturing processes.

Ceramic processing is complicated both by the number of steps required in manufacture (Fig. 1), and by requirements to optimize the processing in the different steps. These factors are often opposed. For example, a fine particle size provides improved plasticity for forming and a higher thermodynamic driving force for sintering; however, electrostatic attraction and van der Waals forces promote agglomeration, ie, the formation of weakly bound particle clusters, and caking, making mixing and packing difficult. Submicrometer particles can be more easily mixed and packed in liquids, but the finer interparticle pore structure results in higher forming and drying stresses, as well as longer forming and drying times.

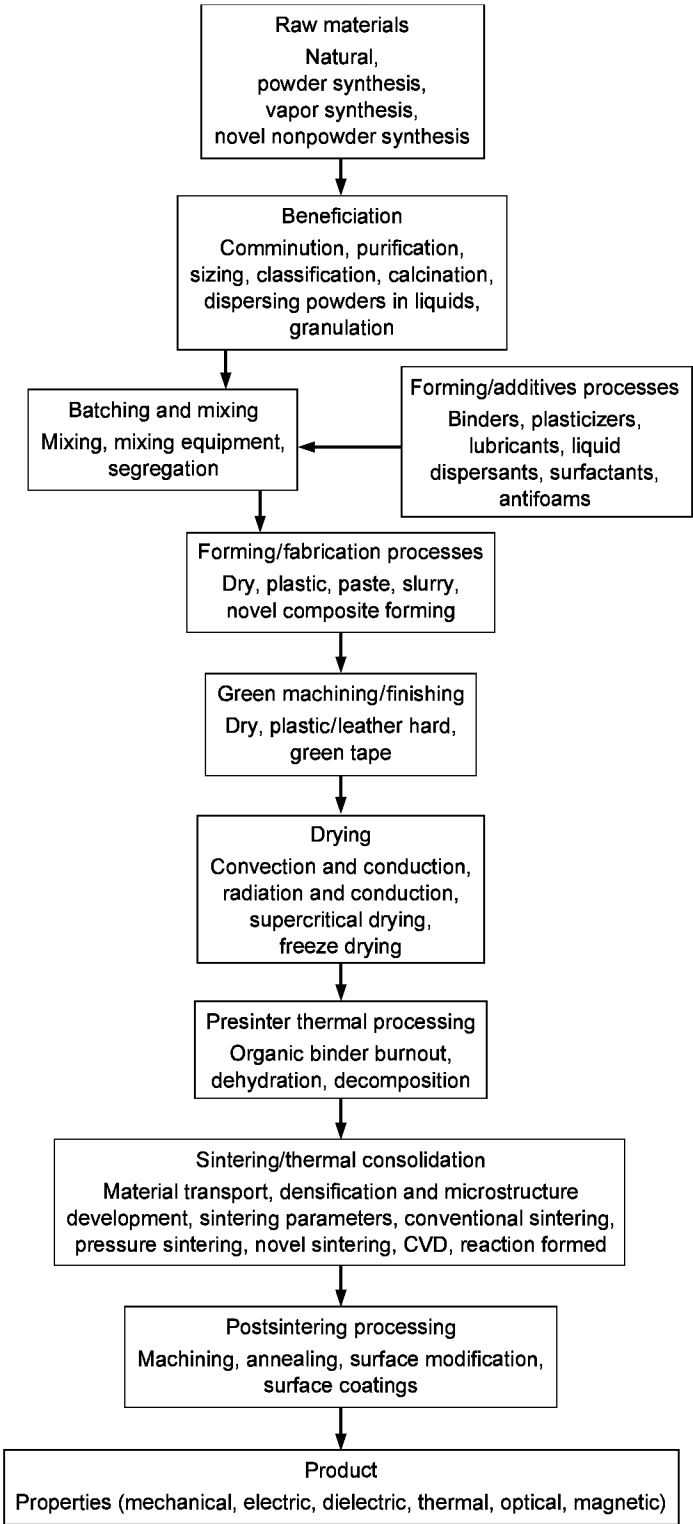


Fig. 1. Flow diagram of the steps and processes involved in manufacturing a ceramic.

Ceramics are basically flaw intolerant materials. Consequently chemical and physical defects can severely degrade properties. Additionally, mistakes are cumulative in ceramic processing and these generally cannot be corrected during sintering and post-sintering processing (as they can be in metals processing, for example). The quality of the product is only as good as the quality of the raw materials used, and the control exercised in each of the

process steps.

Raw Materials

Raw materials for ceramic processing range from relatively impure clay materials (see CLAYS) mined from natural mineral deposits, to ultrahigh purity powders prepared by chemical synthesis. Inexpensive raw materials that cost a few cents per kilogram are typically used in manufacturing the traditional, high volume production ceramics shown in Figure 2, whereas synthesized ceramic powders, whiskers, and fibers costing hundreds of dollars per kilogram are used for advanced ceramics (qv). Chemically and physically beneficiated mined raw materials, eg, bauxite [1318-16-7] (see ALUMINUM COMPOUNDS), comprise the bulk of the oxide raw materials, eg, Al_2O_3 , used in ceramic manufacturing, and make up the middle ground between the two extremes.

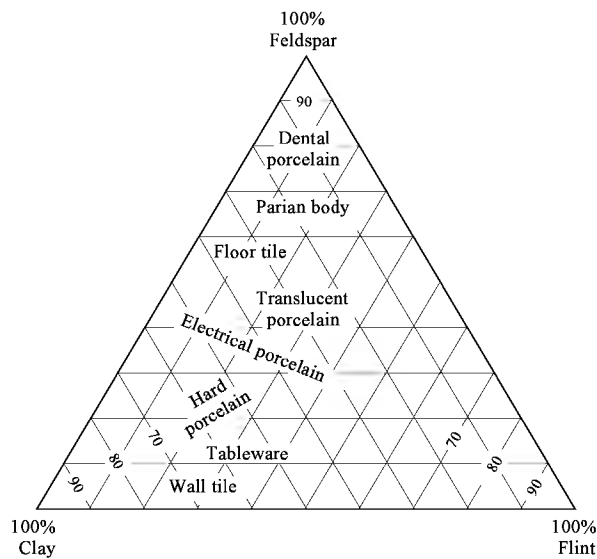


Fig. 2. Examples of traditional ceramics manufactured using traditional ceramic raw materials: clay, flint, SiO_2 , and feldspar.

Natural. Naturally occurring ceramic raw materials (1–11) such as silica [7631-86-9] (qv), SiO_2 , sand, quartz [14808-60-7], or flint [7631-86-9]; silicates eg, talc [14807-96-6], $\text{Mg}_3\text{Si}_2\text{O}_{10} \cdot \text{OH}_2$, wollastonite [14567-51-2], and asbestos [1332-21-4] (qv); and aluminosilicates, eg, clays, feldspars, pyrophyllite [12269-78-2], and sillimanite [12141-45-6], are used extensively as raw materials in the manufacture of traditional ceramics (see Fig. 2). Seawater and brine wells provide another source of ceramic raw materials, eg, magnesium oxide [1309-48-4], MgO (see CHEMICALS FROM BRINE). The principal advantage of naturally occurring raw materials is the low cost; the disadvantage is chemical impurity.

Naturally occurring raw materials are generally found in large, flat-lying mineral deposits near the earth's surface, and are mined using open-pit methods (8–12). Hydraulic mining techniques are also used to mine clays and glass (qv) sands (12) (see MINERAL RECOVERY AND PROCESSING).

Chemically Synthesized Powders. Chemical synthesis provides a means of producing powders for manufacturing advanced ceramics. Disadvantages of chemically synthesized raw materials are expense and difficulties in scale-up and availability. Additionally, ultrafine particle-size powders produced by chemical synthesis pose some unresolved processing problems in the areas of handling and mixing.

Solid State. Ceramic compounds can be formed by reacting constituent oxides and or thermally decomposed salts at an elevated temperature in a solid-state process described as calcination (2,13–17). For example, spinel [1302-67-6], MgAl_2O_4 , can be formed by reacting magnesia [1309-48-4], MgO , and alumina [1344-28-1], Al_2O_3 . Because solid-state diffusion is inherently slow, fine, well-mixed powders are required to ensure that reactions go to completion and that chemical and structural homogeneity are achieved during calcination. Often multiple calcination, grinding, and mixing steps are performed to ensure homogeneity. Purity of the product is limited by the purity of the constituent raw materials, and by the impurities introduced during grinding. Ceramic powders formed by calcination are typically less expensive (<\$1/kg) than those formed by liquid or vapor techniques (~\$25–50/kg), but are also typically less pure and larger in size.

Solution Chemistry. Submicrometer particle size, high purity ceramic powders can be produced by precipitation, solvent evaporation, and solvent extraction from liquid solutions. The solid product is typically a salt that can be calcined at low temperatures, followed by light milling to produce reactive particles for sintering. Solution-derived powders have exceptionally high purity and homogeneity and can be extremely fine in size. Additionally, it is relatively easy to form multicomponent compounds and to add and disperse uniformly small concentrations of dopants, eg, sintering aids, by solution processing. However, chemical precursors are typically expensive, solution processes are not well suited to forming nonoxide ceramic powders, and surface contamination and microporosity common in solution-derived powders often make it difficult to produce dense, optical quality, ie, transparent, ceramics.

Precipitation (2,13–17) techniques employ a combination of nucleation and growth induced by adding a chemical precipitant, or by changing the temperature and or pressure of the solution. Chemical homogeneity is controlled by controlling the rate of precipitation. Heterogeneous precipitation involves the precipitation of a solid of different composition from the solution, and the composition of the precipitate may change as precipitation continues. Coprecipitation involves the simultaneous precipitation of similar size cations in a salt as a solid solution.

Precipitation is commonly performed using water-soluble salts; however, organometallics also provide a good source of high purity reactants for precipitation. Powders can also be formed by mixing reactant oxides in molten salts and precipitating. The calcination step for salt decomposition can be eliminated by precipitating powders in hot, high pressure water, using hydrothermal synthesis (see HYDROTHERMAL PROCESSING).

Solvent evaporation (13–15,17,18) techniques employ rapid drying to produce ceramic powders. Chemical homogeneity can be maintained by rapidly drying isolated, fine (10–100 μm) salt solution droplets produced by atomization, or by microwave or emulsion drying. Aerosol decomposition, also described as spray pyrolysis and evaporative decomposition of solutions, provides a means of enhancing powder production by combining rapid drying, precipitation, and decomposition in a single process similar to spray drying (see EVAPORATION).

Solvent extraction (2,13–15,17) by freeze drying provides another means of maintaining chemical homogeneity in solution-derived powders. Freezing solutions or emulsions prevents chemical segregation and the desired salt is obtained by removing the solvent by sublimation.

Sol-Gel Techniques. Sol-gel powders (2,13,15,17) are produced as a suspension or sol of colloidal particles or polymer molecules mixed with a liquid that polymerizes to form a gel (see COLLOIDS; SOL GEL TECHNOLOGY). Typically, formation of a sol is followed by hydrolysis, polymerization, nucleation, and growth. Drying, low temperature calcination, and light milling are subsequently required to produce a powder. Sol-gel synthesis yields fine, reactive, pseudo-crystalline powders that can be sintered at temperatures hundreds of degrees below conventionally prepared, crystalline powders.

Vapor-Phase Techniques. Vapor-phase powder synthesis techniques, including vapor condensation, vapor decomposition, and vapor–vapor, vapor–liquid, and vapor–solid reactions, employ reactive vapors or gases to produce high purity, ultrafine, reactive ceramic powders. Many nonoxide powders, eg, nitrides and carbides, for advanced ceramics are prepared by vapor-phase synthesis.

Vapor-condensation (2,14,18) involves vaporizing a solid material at high temperature and precipitating a powder by condensation on cooling. Thermal plasmas that operate at several thousand degrees Kelvin at atmospheric pressure and higher can provide the vaporization energy (see PLASMA TECHNOLOGY). Only a very limited number of ceramic powders can be produced by this technique.

Vapor decomposition (14,15) involves drying, decomposing, and vaporizing a spray of salt precursor solution in a plasma, and subsequently nucleating and growing ceramic particles in the vapor. Silicon carbide [12504-67-5], SiC, powder is produced by this method.

Vapor–vapor reactions (14,16,17) are responsible for the majority of ceramic powders produced by vapor-phase synthesis. This process involves heating two or more vapor species which react to form the desired product powder. Reactant gases can be heated in a resistance furnace, in a glow discharge plasma at reduced pressure, or by a laser beam. Titania [13463-67-7], TiO₂, silica, silicon carbide, and silicon nitride, Si₃N₄, are among some of the technologically important ceramic powders produced by vapor–vapor reactions.

Vapor–solid reactions (13–17) are also commonly used in the synthesis of specialty ceramic powders. Carbothermic reduction of oxides, in which carbon (qv) black mixed with the appropriate reactant oxide is heated in nitrogen or an inert atmosphere, is a popular means of producing commercial SiC, Si₃N₄, aluminum nitride [24304-00-5], AlN, and sialon, ie, silicon aluminum oxynitride, powders.

Nonpowder Synthesis. Many ceramic composites (qv) under investigation utilize reinforcing ceramic whiskers or fibers to achieve toughening (19). Whiskers (17,19,20) are produced by vapor-synthesis techniques. SiC whiskers can be produced by the rice hull or vapor–solid (VS) method whereby rice hulls are pyrolyzed to produce a mixture of carbon, C, and SiO₂, and whiskers are produced by directional growth by vapor deposition. The vapor–liquid solid (VLS) or Los Alamos process uses a liquid catalyzed vapor-deposition process to produce SiC whiskers from reagent-grade gases. Whiskers cost several hundreds of dollars per kilogram.

Fibers (17) can be formed by air drag or blow spinning molten precursors, and extruding or drawing gels through a spinneret. Air drag spinning is one of the oldest techniques for manufacturing fibers and uses air jets to draw a fiber from a melt reservoir and shape it. Blow spinning involves blowing a thin stream of compressed air or steam on a molten liquid as it passes through a small opening in the bottom of a melt reservoir. Al₂O₃–SiO₂ fibers are fabricated by blow spinning.

The extrusion process involves extruding, melt spinning, or drawing a controlled viscosity gel through a spinneret, followed by heating to effect gelation and crystallization. Al₂O₃ and Al₂O₃–ZrO₂ fibers are made this way. Nonoxide ceramic fibers have also been produced from amorphous preceramic polymer precursors by melt spinning. Fibers can also be formed indirectly by infiltrating an organic cloth fiber with a ceramic precursor solution, or by depositing a ceramic coating on a fiber preform using chemical vapor deposition (CVD). The desired ceramic fiber product is subsequently formed upon heating.

Although not as expensive as whiskers, fibers are considerably more expensive than powders. Extrusion processed Al₂O₃ and Al₂O₃–ZrO₂ fibers cost \$100–200 kg.

Beneficiation

Beneficiation (2,11,12,21–27) involves a process or series of processes whereby the chemical and or physical properties and characteristics of raw materials are modified to render the raw material more processible. The extent of beneficiation is determined by a combination of the starting raw materials, the processing scheme, the desired properties of the product, and economics. Powder cost increases with increased beneficiation; consequently, low value-added clay raw materials used to produce inexpensive structural clay products typically undergo a minimum of beneficiation, whereas higher value-added alumina powders undergo more extensive beneficiation.

Chemically synthesized materials also often undergo some form of beneficiation. Beneficiation processes for chemically synthesized ceramics are sometimes incorporated in the forming process such as in aerosol decomposition, where solvent evaporation and salt decomposition occur sequentially in a single operation.

Comminution. Particle size reduction by crushing and grinding milling, otherwise known as comminution, is used extensively in ceramic processing to liberate impurities, break up aggregates, modify particle morphology, modify particle size distribution, improve processability during the mixing and forming operations, and produce more reactive powders for sintering (12,22,23). Crushing (11,12,21,22) operations are used for coarse grinding; milling (22–25) operations are used for fine grinding.

Primary crushers (11,12,21) are designed to reduce relatively large, up to 0.3 m diameter, mined material down to centimeter size particles. Secondary crushers (11,12,21) employ compression and impact compression to produce millimeter size particles. Natural raw materials processors typically supply material that has been processed through a primary and secondary crusher, and is often sized by screening.

Higher value-added, naturally occurring raw materials are generally ground to micrometer sizes by the raw materials supplier; however, additional grinding may be necessary prior to manufacturing. Micrometer size powders are produced by grinding millimeter and smaller size particles in a ball mill (2,22,23), vibratory mill (2,22), attrition mill (2,22), or fluid energy mill (2,23). Both particle size and size distribution decrease during grinding. In general, wet milling is more efficient than dry milling, producing a finer, typically submicrometer median particle size powder having a narrower size distribution. The practical lower particle size limit that can be achieved by milling is ~1.0 μm.

Ball milling (2,22,23), also referred to as jar or pebble milling, may be the most popular means of fine grinding ceramic powders. Ball milling can be performed wet or dry and as a batch or continuous process using spherical or cylindrical grinding media. Milling with media that is rod shaped is referred to as rod milling. Approximately 1 wt % grinding aid is generally added to minimize agglomeration during dry milling, and <1 wt% of a dispersant can be used to inhibit flocculation during wet milling. Water or alcohol are commonly used as the milling liquid.

Purification. Alumina, Al₂O₃, is produced by the Bayer process (1,9) (see ALUMINUM COMPOUNDS) which involves digestion followed by precipitation and calcination. High purity magnesia is extracted from natural brines and seawater by precipitation and calcination (1,9).

Soluble impurities can be extracted by washing with deionized or distilled water followed by filtration (1,12,26). Powders prepared by wet chemical synthesis are often washed and filtered for purification prior to use. The dewatering (qv) process can be enhanced by pressure filtration. Organic solvents can be used to remove water-insoluble impurities and wash-water sensitive materials.

Chemical leaching (1,12) with acids is used to extract metal contamination. High purity zirconia, ZrO₂, is produced by the caustic fusion of zircon [14475-73-1], ZrSiO₄, followed by the chemical removal of silica. Chemical leaching is generally followed by washing.

Magnetic separation (12,26) is used to extract magnetic impurities such as iron and iron minerals from raw minerals (see SEPARATION, MAGNETIC). Magnetic separation can be performed on dry powders and fluid slurries passing through an intense magnetic field. Froth flotation (qv) (12,26) can be used to separate intermixed raw materials and to separate the desirable material from the gangue.

Sizing. Sieve sizing (2,12,26,27) utilizes gravitational forces acting on particles translating across a screen (see SEPARATION, SIZE). The process can be enhanced by vibrating the sieves. Dry forced air and sonic sieving are used to size dry powders from 850 to 37 μm in size. Wet sieving eliminates electrostatic particle–particle and particle–sieve attractive forces to size particles down to ~5 μm.

Classification. Classification (2,12,26,28) or elutriation processes separate particles by the differences in how they settle in a liquid or moving gas stream. Classification can be used to eliminate fine or coarse particles, or to produce a narrow particle size distribution powder. Classification by sedimentation involves particle settling in a liquid for a predetermined time to achieve the desired particle size and size distribution or cut. Below ~10 μm, where interparticle forces can be significant, gravitational-induced separation becomes inefficient, and cyclone and centrifugation techniques must be used. Classification also separates particles by density and shape. Raw material separation by differential sedimentation is commonly used in mineral processing.

Calcination. Calcination (1,2,29) involves heat treating a powder or mixture of powders at a temperature well below its melting point to effect decomposition, ie, to liberate unwanted gases and or chemically bound waste, solid-state reactions, and structural transformations to produce the desired composition and phase product. For example, water is liberated and the crystallographic structure changes when α-Al₂O₃·3H₂O is calcined to form α-Al₂O₃.

Calcination or dead burning is used extensively to dehydrate cements (qv) and hygroscopic materials such as MgO, and to produce a less water sensitive product. Calcination is also used to decompose metal salts to base oxides and to produce multicomponent or mixed oxide powders for

manufacturing advanced ceramics. For example, barium carbonate, BaCO₃, is decomposed to form barium oxide, BaO, and fine particles of BaCO₃ and TiO₂ are intermixed and calcined to produce barium titanate [12047-27-7], BaTiO₃, powder for ceramic capacitors for solid-state electronics.

Calcination can be completed in an inclined rotary calciner, a heated fluidized bed, or by simply heating a static bed of powder in a refractory crucible.

Dispersing Powders in Liquids. The preparation of a slurry by dispersing a solid in a liquid entails (1) wetting the solid by the liquid; (2) breaking down flocs; and (3) stabilizing the system to prevent flocculation (30,31). Dispersing aids such as deflocculants and wetting agents are usually added to the liquid prior to mixing the powder with the liquid.

Slurry processing has a distinct advantage over dry, semi-dry, and plastic forming techniques in that the liquid provides an improved medium for mixing. Additionally, liquids eliminate electrostatic attraction forces between fine particles and particle surface charges and agglomeration can be controlled. The disadvantage is that the liquid has to be removed before firing. This increases the processing time and cost and can create problems with shape distortion and cracking during drying.

Granulation of Powders. To improve flow, handling, packing, and compaction, dry powders are typically granulated (2,32). Agglomerates or granules of controlled size, shape, and strength are formed by directly introducing a liquid binder solution during powder stirring mixing, or by spray drying.

Direct mixing (32) by compaction using a tableting die, briquetting rolls, a Muller mixer, extrusion, or spray granulation produces dense, hard, strong granules. An auger extruder or kneader is used to produce more plastic granules. Nearly spherical granules can be formed by spraying a liquid or binder solution into an agitating powder, such as a rotating pan, ribbon, double planetary, or V-cone mixer. The more intense the mixing action and higher the temperature, the smaller the granules.

Spray drying (2,32) provides a means of indirectly forming dense, homogeneous, nearly spherical granules from a slurry. The process involves atomizing a high solids content slurry through a pressure nozzle or rotary atomizer into a conical chamber with a cocurrent or countercurrent stream of heated air that dries the atomized droplets to form >20 μm, free-flowing granules. The product is collected in a container at the base of the spray dryer. Spray drying is widely used to prepare a variety of granulated, free-flowing ceramic powders with excellent compaction behavior for dry powder pressing operations.

Forming Additives/Processing Aids

Forming additives or processing aids (2,33–37) are commonly used to render ceramic powders more processible. Binders and plasticizers (qv) are typically added to improve or aid dry powder and plastic forming, whereas deflocculants, surfactants (qv), and antifoams are commonly used in slurry processing.

Binders. Binders (35,37,38) are used to impart strength to a green or unfired ceramic body for handling and green machining. Binders are polymer molecules or colloids (qv) that adsorb on particle surfaces and promote interparticle bridging or flocculation. Binders are used extensively in dry-pressing operations and are also added to plastic extrusion bodies and pastes. With the exception of tape casting, where a plasticized binder is required to produce flexible green tape, binders are generally avoided in slurry forming operations.

Binder selection depends on the ceramic powder, the size of the part, how it is formed, and the green density and strength required. Binder concentration is determined by these variables and the particle size, size distribution, and surface area of the ceramic powder. Three percent binder, based on dry weight, generally works for dry pressing and extrusion.

Binders such as poly(vinyl alcohol) (PVA) that form hard ceramic granules, produce free-flowing powders that are well-suited for automated pressing operations and yield strong bodies. Plasticizers and or lubricants (see LUBRICATION AND LUBRICANTS) can be added to hard binders to reduce the forming pressure and die wear. Wax binders such as poly(ethylene glycol) (PEG) form soft ceramic granules which yield lower strength, higher green density bodies on forming. Hard and soft binders can be combined to develop binder systems tailored to a given process and product.

Specialty binders may be used in novel or unique forming operations. Cross-linking polymers are used to induce gelation in gelcasting. Thermoplastic resins such as polyethylene and polystyrene often comprise the bonding matrix in injection-molded ceramic parts. Phosphate chemical bonds are used in forming specialty refractories (qv), and chemical hydration is employed in setting hydraulic cements. Preceramic polymers that decompose to a ceramic on heating serve as binders to provide green strength for handling and machining.

Plasticizers. Plasticizers (36–38) are often added to a binder to reduce cross-link density and increase flexibility. Plasticizers improve toughness, springback, and flexibility, but degrade overall green strength. Additionally, plasticizers can increase the sensitivity of a binder system to moisture.

Examples of plasticizers include adsorbed water and ethylene glycol for vinyl binders, stearic acid and oleic acid for wax binders, glycerine and ethylene glycol for clay bodies, and molten oils and waxes for thermoplastic polymers used in injection molding.

Lubricants. Lubricants (36,38) are added to lower frictional forces between particles, and between particles and die surfaces to improve compaction and minimize die wear. Typically <1 wt % of a lubricant is required for forming, and usually only with hard binders. Stearic and oleic acids are good lubricants for ceramics.

Individual particle surfaces can be lubricated by an adsorbed film that produces a smoother surface and or decreases interparticle attraction. A plasticized binder may serve this purpose. Forming surfaces can be lubricated by coating with a film of low viscosity liquid such as water or oil. Die surfaces can also be coated with a solution of stearic acid dissolved in a volatile liquid that rapidly evaporates to leave a lubricating film.

Fine particles having a laminar structure and smooth surfaces are effective solid lubricants for rough surfaces and at high pressure. Graphite, boron nitride, BN, and talc are good solid lubricants; however, solid inorganic lubricants do not burn out during sintering and may affect the microstructure and properties of the finished product.

Liquids. Liquids (33) are common forming additives in plastic, paste, and slurry processing. In plastic forming operations, the liquid aids forming and serves as the binder plasticizer for the system. In pastes and slurries, other additives are also dissolved or dispersed in the liquid solvent. Water is a good, inexpensive solvent that can be recycled. Organic liquids such as alcohols are used to process water-sensitive materials and to dissolve water-insoluble forming additives, however, at considerably more expense.

Deflocculants. Deflocculants (34), dispersants (qv), or anticoagulants are added to slurries to improve dispersion and dispersion stability. Dispersants break up flocs in a slurry by lowering van der Waals interparticle forces. Deflocculants adsorb on particle surfaces and prevent the approach of particles either by electrostatic or steric stabilization. Deflocculation by electrostatic stabilization is common in clay slurries, as well as with ceramic particles dispersed in polar liquids such as water.

Monovalent cations are good deflocculants for clay–water slips and produce deflocculation by a cation exchange process, eg, Na⁺ for Ca²⁺. Low molecular weight polymer electrolytes and polyelectrolytes such as ammonium salts (see AMMONIUM COMPOUNDS) are also good deflocculants for polar liquids. Acids and bases can be used to control pH, surface charge, and the interparticle forces in most oxide ceramic–water suspensions.

Oleic acid is a good deflocculant for oxide ceramic powders in nonpolar liquids, where a stable dispersion is created primarily by steric stabilization. Tartaric acid, benzoic acid, stearic acid, and trichloroacetic acid are also deflocculants for oxide powders in nonpolar liquids.

Surfactants and Antifoams. Surfactants (33) or wetting agents can also be added to a slurry to improve dispersion. A wetting agent lowers the surface tension of the liquid, lowering the solid–liquid interfacial energy, which favors the liquid coating the solid. Antifoams (36) are added to slurries to remove trapped gas bubbles from the liquid (see DEFOAMERS). Commercial agents include fluorocarbons, dimethylsilicones, stearates, and high molecular weight alcohols and glycols. Typically, less than a few percent of an antifoam agent is required to prevent foaming.

Batching and Mixing

Mixing (24,39) is used to combine the constituents of a ceramic body to produce a more chemically and physically homogeneous system for forming (see MIXING AND BLENDING).

Convection, Shear, and Diffusion Mixing. Mixing is accomplished by material transport by convection, shear, and diffusion (39). Feeding devices, stirring, and baffles all produce material flow that contributes to convection. Material flow between surfaces moving at different velocities

produces shear stresses that can break down agglomerates and mix viscous materials. Turbulent flow produced by eddy currents, cavitation, impact, and sonic vibration contribute to diffusive mixing, which also breaks down agglomerates.

Segregation. Segregation (24) or separation in mixtures of dissimilar particles can occur during storage and handling, resulting in macroscale heterogeneities in the product. Segregation can be minimized by minimizing size differences, storage and handling after mixing, and individual particle motion during mixing (see POWDERS, HANDLING).

Forming/Fabrication Processes

Ceramic forming involves consolidation and molding of ceramic powders to produce a cohesive body of the desired size and shape. Ceramic forming operations (38,40–66) are conducted with dry powders, plastic bodies, pastes, and slurries.

Dry Forming. Dry powders can be simultaneously compacted and shaped by pressing in a rigid die or flexible mold. Pressing (38,40–42,48–52) is the most widely used forming process in ceramics manufacturing. Microelectronic chip carriers, capacitors, spark plug bodies, cutting tools, and ceramic tiles are manufactured by powder pressing.

Powder pressing involves three general stages including: (1) filling the die or mold; (2) compacting and shaping the powder; and (3) extracting the pressed part from the die. When the pressing pressure is released, the dimensions of the powder compact and die increase or springback. Differential springback between the compact and mold aids extraction of the pressed part; however, excessive differential springback >0.75 linear % can generate catastrophic stresses that create defects or destroy the compact. Pressing defects can be minimized by using granulated powders and appropriate additives, and by controlling the pressing pressure, pressurization rate, and depressurization rate used in forming.

For reproducibility and rapid processing, pressing powders should be free-flowing, have a high bulk density, be comprised of deformable granules, cause minimal die wear, and not stick to die surfaces.

Dry Pressing. Dry or die pressing (38,40–42,45,48–50) which involves compacting a powder between two plungers in a die cavity, is a versatile technique for fabricating relatively uniform thickness and axial symmetric powder compacts. Manual dry pressing is used to form limited numbers of cylindrical pellets of single-phase and composite powders for sintering experiments. Automated dry pressing is capable of producing 5000 parts per minute.

Dies are made of hardened steel, specialty steels, and carbides (qv) or other structural ceramics, eg, SiC, Al₂O₃. Single-action, ie, moving top plunger, double-action, ie, moving top and bottom plungers, and floating die, (ie, moving top plunger and die body, pressing assemblies are used. In automated processes, the pressure is typically in the range of 20–100 MPa (3–15 × 10⁶ psi); however, manual die pressing operations may be carried out at pressures as high as 200 MPa (29 × 10⁶ psi). Die wear, ejection pressure, and differential springback all increase with pressing pressure.

Nonplastic ceramics are typically dry pressed using <4 vol % water. Plastic ceramics can be formed by semidry pressing using 10–15 vol % water. Warm dry pressing with heated platens at <200°C is used to fabricate multilayer substrates from tape cast green tape for microelectronic packaging.

Isostatic Compaction. Isostatic pressing (38,40–42,45,51,52), which is also known as isopressing, hydrostatic pressing, and cold isostatic pressing (CIP), provides a means of manufacturing complex shapes such as tubes and spark plug bodies, and larger volume parts that are not easily dry pressed. Because the compacting pressure is applied uniformly over a larger free surface area, pressing gradients are typically less severe. Typically, a flexible mold or bag is filled with a granulated powder, sealed, and placed in a gas- or liquid-filled pressure chamber and pressurized to 5–200 MPa (1–29 × 10⁶ psi) to compact the powder. Because gas cannot escape during the isopressing operation, molds are typically deaired prior to pressing. Also, to improve the filling density, molds may be filled on a vibratory or tapping table. Both wet and dry bag techniques are employed in isopressing; although only the dry bag technique is suited to automation.

Isopressing molds are typically comprised of synthetic rubber, polyurethane, or silicone rubber with rigid steel fixtures and mandrels. Because of the relatively high springback of flexible mold materials, controlled, slow, depressurization is required below 2 MPa (3 × 10⁵ psi) to control mold expansion and to avoid damaging the compact on extraction. Isopressing is typically performed at ambient temperature; however, by heating the pressurizing liquid, warm isostatic pressing (WIP) can be accomplished. WIP is being investigated as an improved technique for laminating multilayers of tape cast green tape to produce microelectronic packages.

Vibratory Compaction. Vibratory compaction (38,53) provides a means of forming irregular shape compacts from ungranulated powders. Under agitation, a powder bed tends to rearrange to a configuration of closest packing. The amplitude and frequency of vibration required for compaction are dependent on the size and size distribution of the particles present, and the size of the compact, and are determined experimentally.

Plastic Forming. A plastic ceramic body deforms inelastically without rupture under a compressive load that produces a shear stress in excess of the shear strength of the body. Plastic forming processes (38,40–42,54–57) involve elastic–plastic behavior, whereby measurable elastic response occurs before and after plastic yielding. At pressures above the shear strength, the body deforms plastically by shear flow.

The cohesive strength required for plastic deformation is provided by capillary pore pressure and flocculation bonding. Plastic clay bodies are typically flocculated by the colloidal clay particles present in the system, whereas nonplastic ceramics can be flocculated with an organic binder. In clay bodies, submicrometer colloidal clay particles coat larger particles, and shear flow occurs between the larger particles in zones of oriented clay and finer nonplastic particles lubricated by interparticle water. In nonclay ceramic bodies plasticized with organic binders, the organic molecules play the role of the colloidal clay particles.

The dimensional tolerances of parts formed by plastic deformation are typically not as good as those in parts formed by dry powder pressing.

Extrusion. Extrusion (38,40–42,54,55) is widely used in manufacturing structural clay products, including sewer pipe, chimney flues, bricks, and tiles. Additionally, refractory tubes and rods, and cordierite catalyst supports for catalytic converters in automobiles having 30–60 openings per square centimeter are formed by extrusion. Clay and talc bodies typically contain 12–20 vol % water, and can be extruded without a lubricant. Nonplastic ceramic powders require a plasticizer for extrusion. The higher the forming pressure, the lower the concentration of liquid required for extrusion, and the shorter the drying time and the lower the drying shrinkage. Extrusion pressures of up to 4 MPa (6 × 10⁵ psi) are used to extrude porcelain bodies, whereas pressures up to 15 MPa (2 × 10⁶ psi) are used to extrude ceramic powders having organic plasticizers.

Extrusion involves: (1) feeding plastic material into a chamber; (2) material consolidation and flow into the barrel, through the forming die and the finishing tube; and (3) ejection. A typical extruder may have a pug mill for additional mixing, and a vacuum chamber to deair the plastic body prior to extrusion. Dies are specially designed to generate sufficient back pressure to heal defects created during forming.

Both piston and auger type extruders are used in plastic forming. The former provide maximum control of the extrusion pressure and rate and are good for forming large parts. The latter provide a maximum extrusion rate without excess power requirements and are desirable in the continuous production of simple clay ware.

Defects in extruded bodies typically include: insufficient strength or rigidity from too much water or insufficient organic binder; cracks or delaminations because of excess differential springback, hard inclusions, or agglomerates from poor mixing; surface blisters from the expansion of dissolved air; surface delaminations created by slip-stick wall friction; nonuniform flow from improper die design; laminations produced by divided flow as a result of improper die design; gradients in extrudate stiffness; and curling on drying from differential drying.

Jiggering. Jiggering (38,40,54) is one of the most widely used, cost effective, soft plastic forming techniques used in ceramic processing for manufacturing small, simple, axial–symmetrical whiteware ceramics including cookware and fine china, and electrical porcelain. Jiggering involves shaping a plastic clay body on a spinning porous plaster mold using a water-mist or steam-lubricated shaping tool. The shaping tool initially deforms the clay mass to the shape of the mold and subsequently creates a smooth surface finish. The mold and shaped part are then set aside and separation of the mold and part is accomplished by differential drying. Hand molding operations are conducted at 300–400 rpm; 500–1200 rpm are used in automated jiggering processes. Automated, highly mechanized jiggering operations can produce 1000 pieces per hour per line.

Powder Injection Molding. Powder injection molding (PIM) (38,42,45,54,56,57) provides an economical means of mass producing small, near-net, complex shapes. PIM involves injecting a hot ceramic and polymer binder mixture into a cooler die to form the desired shape, then extracting and deburring the part, and removing the binder. The binder concentrations for PIM range from 30 to 50 vol % and must be high enough for good flow during molding, but low enough to avoid debinding problems and excessive debinding times.

PIM is not cost competitive with die compaction for simple or axial–symmetric shapes. It is limited to small (<10 cm) shapes and is extremely

process sensitive. Additionally, PIM tooling is expensive.

Paste Forming. Ceramic pastes (58), often associated with thick-film printing operations, consist of a ceramic powder, a sintering aid such as borosilicate glass, and an organic vehicle comprised of a solvent, dispersant, plasticizer, and high molecular-weight binder. Ceramic thick-film pastes are used for decorating traditional ceramic tableware and to form capacitors and dielectric insulator layers on rigid substrates for microelectronic packaging.

Slurry Forming. Slurries are used in ceramic casting operations (38,40–42,59–66) and slurry formation is perhaps the most important step. A good slurry is well dispersed and free of air bubbles and foaming; it has a high specific gravity; it has good rheological properties for casting; the solid particle settling rate in the slurry is low; and it is chemically stable. Additionally, when dry, the cast should possess sufficient strength for subsequent finishing and handling before firing.

The liquid vehicle in a slurry should: have a low vapor pressure for liquid extraction and drying; be compatible with the solids and casting mold; be inexpensive; and be capable of dissolving and dispersing deflocculants and other additives. Distilled or deionized water is generally used as the liquid vehicle, however, organic liquids must be used for such moisture sensitive oxide powders as CaO and MgO, and for oxidation sensitive nonoxide powders, eg, AlN.

A high solids concentration is desirable to minimize the amount of time and energy required for forming and to minimize drying shrinkage. Using deflocculants, fluid slurries can be made using as little as 15–20 vol % liquid.

Slip Casting. Slip casting (38,40–42,45,59–62), the process in which a cast is formed from a slurry using a porous mold, is used to form sinks and other sanitary ware, figurines, refractory crucibles, porous thermal insulation, fine china, and complex shape structural ceramics such as multivane rotors.

Slip casting begins by pouring a stable slurry into a porous mold. The capillary suction of the porous mold draws the liquid from the slurry to form a higher solids content, close-packed cast on the inner surface of the mold. Wall thickness increases with the square root of forming time, and with sufficient time a completely solid cast can be formed. After a fixed time the excess slurry is drained from the cast (drain casting). Initial drying occurs in the mold, and the resultant cast shrinkage and strengthening aids in separating the cast from the mold. A mold-release agent, such as an alginate, graphite, a silicate, talc, silicone, or olive oil, can be used to enhance the removal of the cast from the mold. Inexpensive plaster molds comprised of 40–50 vol % porosity are typically used in slip casting.

Casting slips are typically pseudoplastic (<2 Pas at a shear rate of 1–10 s^{–1}) for good mold filling and to allow the escape of gas bubbles. Additionally, the concentration of solids must be high enough to minimize settling during casting. Solid casting is generally conducted with slightly higher viscosity and higher solids content slips.

To control the concentration of submicrometer colloidal particles to <30%, clay slips are typically used in the partially deflocculated state. A coagulant can be added to a deflocculated clay slip immediately preceding casting to induce partial flocculation. Slurries for casting oxides, nitrides, and carbides are generally at least partially deflocculated. A fraction of a percent of organic binder increases the pseudoplasticity of the slurry and strength of the cast; too much binder can clog the plaster molds and decrease the rate of casting.

Casting rate can be enhanced through the use of vacuum casting (38,59), ie, by increasing the pressure gradient, or through pressure casting (38,59), ie, by decreasing the slurry viscosity, eg, by heating, or by centrifugal casting. Each enhance the rate of liquid flow from the slurry into the mold and decrease the casting time from hours to minutes, decrease the concentration of water in the cast and the shrinkage on drying from several percent to ~1%, and yield higher green density casts that shrink less on firing. Additionally, centrifugal forces created by spinning the mold, and or vibration can be used to enhance slurry flow and to ensure good filling of complex molds.

Disadvantages of vacuum, pressure, or centrifugal casting include higher costs because of specialty equipment and specialty molds, and density gradients in the casts that result from the higher pressure gradients during forming.

Gelcasting. Gelcasting (63) is a novel method of fabricating particulate bodies from ceramic slurries. Gelcasting employs *in situ* polymerization of organic, eg, acrylamide (qv), monomers to produce a gel structure that binds individual particles together to form a cohesive body. Net and near-net complex shapes such as turbine rotors can be cast in a relatively short period of time, and the high (up to 62 vol %) solids concentrations improve the homogeneity of the cast and contribute to lower and more reproducible shrinkage during drying and sintering. Gelcast parts also have excellent strength for handling and green machining.

Tape Casting. Tape casting (38,45,59,64–66), doctor-blading, or knife coating involves forming a thin film of slurry of controlled thickness by flowing a slurry beneath the knife edge of a doctor blade onto a support surface. Tape casting is an economical means of forming thin (0.02–2.0 mm), uniform thickness, smooth surface, flexible, green ceramic sheet or tape that can subsequently be cut and stacked to form multilayer ceramics for multilayer capacitors and dielectric insulator substrates (see also CERAMICS AS ELECTRICAL MATERIALS).

The thickness of the tape is controlled by the slip characteristics, the height of the doctor blade, the casting rate, and the pressure head of the slip reservoir behind the doctor blade. Slip viscosities in the range of 1–5 Pas (10–50 P) are used to cast tapes at 5–100 cm/s. To achieve the desired strength and flexibility in the green tape, tape casting slurries contain more binder than those used in slip casting, as well as a plasticizer to ensure flexibility.

Tape can be cast on a stainless steel table or belt, glass plate, or a Mylar, Teflon, or cellulose acetate film carrier. The tape should adhere to the carrier sufficiently to prevent curling, but should be easily removable. In a continuous casting process, the tape is dried by air flowing 1–2 m/min counter to the casting direction. A typical dry green tape contains approximately 35 vol % organics, 50% ceramic powder, and 15% porosity.

Specialty Casting Techniques. Thixotropic casting (59) processes involve slurries comprised of a gelling, reactive, or hydraulic binder in which yield strength and viscosity increase with time. Thixotropic slurries are used for gunning or troweling castable refractory wall liners, preparing refractory shapes and molds for metal casting operations, obtaining dental impressions and filling cavities, and producing concrete structural materials.

Electrophoretic casting (38,59) is accomplished by inducing controlled migration of charged particles under an applied electric field to deposit on a mandrel. Thin tubular shapes and coatings of limited thickness are formed using this technique. Electrophoretic deposition (EPD) is also used to manufacture thin wall, solid β -alumina [12005-16-2], NaAl₅O₈, electrolytes for sodium–sulfur batteries.

Freeze casting (59) is a hybrid of slip casting, gel casting, and freeze drying in which a slurry is poured into a rigid rubber mold, frozen, and the frozen liquid is removed by sublimation, ie, by freeze drying (see CRYOGENICS).

Novel Composite Forming Techniques. Particulates, whiskers, or fibers, can be used to improve the toughness of ceramics (19). Composites (qv) or multicomponent ceramic bodies containing second-phase reinforcing particulates, whiskers, or fibers can be processed by the dry powder, plastic, and slurry forming techniques described, but with considerably more difficulty. Challenges in composite processing include: uniformly dispersing the reinforcing phase; maintaining the desired orientation of the reinforcing phase within the matrix; and uniformly packing the matrix particles about the reinforcing phase.

Particulate Composites. In addition to the geometric obstacles to mixing dissimilar shape and size particles, there are also chemical barriers that must be overcome in processing composites, requiring novel techniques.

Coatings (qv) offer one means of reducing or eliminating the differences in dissimilar materials. For example, a silica coating on alumina allows alumina and silica particles to be dispersed together in water at the same pH. Likewise, oxide-resistant coatings on carbide and nitride powders render them compatible for coprocessing with otherwise incompatible oxide ceramics. Coatings can also be employed to aid the processing of whisker and fiber reinforced composites.

Infiltration (67) provides a unique means of fabricating ceramic composites. A ceramic compact is partially sintered to produce a porous body that is subsequently infiltrated with a low viscosity ceramic precursor solution. Advanced ceramic matrix composites such as alumina dispersed in zirconia [1314-23-4], ZrO₂, can be fabricated using this technique. Complete infiltration produces a homogeneous composite; partial infiltration produces a surface modified ceramic composite.

Preceramic polymer precursors (45,68) can be used to make ceramic composites from polymer ceramic mixtures that transform to the desired material when heated. Preceramic polymers have been used to produce oxide ceramics and are of considerable interest in nonoxide ceramic powder processing. Low ceramic yields and incomplete burnout currently limit the use of preceramic polymers in ceramics processing.

Whisker and Short Fiber Composites. Whiskers and short fibers tend to align during forming, leading to anisotropic properties and large

flaws in the product. Commercial whisker and fiber reinforced ceramics are formed by dry or isostatic pressing. Slip casting, tape casting, and injection molding processes are under development. Ceramic short fiber mat is manufactured in the dry mat process (42) by blowing a dispersion of 6–25 mm long staple fibers onto a moving belt by a stream of air and reacting it in a heated zone. The mats are resin reinforced and are limited to a thickness of 1–3 mm. The wet mat process (42) employs paper-making technology to fabricate denser, thicker web mat with staple fiber. Fibers and binder dispersed in water are cast, filtered, and dried in ovens (see PAPER).

Continuous Fiber Composites. Textile manufacturing (42) techniques are used to fabricate continuous fiber ceramics and ceramic composites (see TEXTILES). Weaving (42) techniques can be used to manufacture ceramics and ceramic cloths having continuous monofilament fibers (qv) and fiber bundles (yarn). Complex parts can be woven with a high volume fraction of fiber; however, the process is slow and expensive. Complex, three-dimensional structures can be formed by multidirectional winding (42) continuous fiber on a mandrel. Rod, bar, tube, or sheet can be fabricated by pultrusion (42), in which a continuous fiber bundle is drawn through a bath of matrix solution that coats the fibers, through a card screen, and then through a heated die.

Prewave fabric to ceramic fabric (42) uses conventional cloth fiber as a preform of the desired shape that is formed by weaving, and then the weave is impregnated with a precursor solution of the desired ceramic. Zirconia ceramic cloth is formed this way. Impregnation (42) provides a means of fabricating polymer-filled, continuous ceramic fiber composites. Laminates of alumina fibers in a polymer resin matrix have been formed that have a thermal conductivity approaching that of alumina in the in-plane direction, and a dielectric constant approximating that of the polymer in the out-of-plane direction. Such composites have potential application in advanced microelectronic packaging.

Green Finishing/Machining

After forming, green finishing or machining is often required to eliminate rough surfaces, smooth forming seams, trim, and modify the size and shape of the green body in preparation for sintering (38,40,45,58).

Surface Grinding or Turning. Surface grinding and turning (38,40,45,58) on a lathe is used to form contours in ceramic spark plug bodies and high tension porcelain insulators (qv), to machine threads, and to fabricate complex shape bioceramic implants. Typically, the strength of the green part must be >2 MPa (>3 × 10⁵ psi), and the tool force for grinding must be carefully controlled to avoid overstressing the relatively weak, green ceramic part during machining.

Blanking, Punching, and Laminating. Blanking, punching, and laminating (45,58,64–66) processes are used to form ceramic multilayers from tape cast green tape. Blanking, coining, or stamping is used to cut or form the desired substrate size and shape, large diameter holes or vias >0.5 mm, and cavities. Smaller vias are punched in a subsequent operation. To form a multilayer ceramic, several layers are stacked together and laminated by uniaxial or biaxial pressing at 3–30 MPa (4–40 × 10⁵ psi) between platens at 50–80°C. Warm isostatic pressing can also be used. To compensate for particle alignment and texture in the cast tape, and to minimize shrinkage anisotropy and warping during drying and sintering, alternating layers in the laminate are rotated 90° to the casting direction during stacking. An alignment die can be used to preserve via alignment during lamination. Final shaping and punching can be performed after lamination as necessary.

Drying

For economical reasons, drying (38,41,45,69–73) should be as fast as possible; however, to avoid differential shrinkage that can result in cracking, warping, and shape distortion, drying must be carefully controlled. Generally, larger parts containing more liquid require longer and costlier drying.

Convective And Conduction Drying.

Air Drying. Air drying is the most common means of drying ceramics (69–73). Circulating hot air supplies heat to the ware to aid evaporation and compensate for evaporative cooling as it removes vapor from the ware surface. The drying rate is determined by two factors: the rate of liquid evaporation and the rate of liquid migration to the drying front.

In a saturated body, drying first occurs at a constant rate by the evaporation of the liquid film surrounding individual particles at the ware surface. If liquid migration cannot keep pace with evaporation, the drying front moves into the bulk of the ware, where drying continues by evaporation from the menisci of the liquid within the pores. During this later stage, falling rate period, the rate of drying continuously decreases with decreasing liquid content. During initial-stage drying, flowing air lowers the relative humidity and thins the boundary layer to enhance evaporation.

Most shrinkage occurs during initial-stage drying. Drying shrinkage can be reduced by lowering the concentration of liquid, decreasing the film thickness, decreasing the concentration of fines and plastic materials, and by adding nonplastics.

Controlled Humidity Drying. Controlled humidity drying (41,69–71) is used to minimize the moisture gradient and stresses during drying, and to optimize the drying rate. A high humidity atmosphere allows for rapid heating of moist ware without creating catastrophic drying stresses. After initial-stage drying, the humidity is rapidly decreased. Humidity controlled drying can reduce drying times from days to hours.

Air Drying Equipment. Tunnel kiln dryers (70) are long furnaces comprised of several zones of different temperature, humidity, and air flow through which the ware travels on a moving car or belt. These kilns afford continuous processing. Periodic kiln cross-circulation dryers (70) are box furnaces in which ware is stacked on permanent racks or on a car that can be shuttled in and out of the furnace. Fans or jets are used to circulate heat uniformly through the ware. The process is not continuous, but production rates can be enhanced by shuttling multiple cars.

Radiation and Conduction Drying. The rate of drying is often determined by the rate of forming and firing. The rate of drying ceramic ware processed with water can be enhanced by using microwave (69) or infrared (41,70) radiation. Radiation drying techniques can reduce drying times from hours to minutes.

Microwave Drying. Microwave radiation drying (45,64) (see MICROWAVE TECHNOLOGY) is excellent for drying porous molds and porous refractories without shrinkage damage, for drying bulk powders without forming agglomerates, and for uniformly drying large volume bodies. Microwave drying is cost effective at or below 5–10 vol % water, and can be used in combination with conventional controlled humidity forced air drying to be economical at higher water concentrations.

Infrared Drying. Infrared drying (41,70) using 4–8 μm electromagnetic radiation supplied by ir lamps is used to rapidly dry thin ceramic ware, such as china formed by jiggering, tape cast ceramic sheet, ceramic substrates, thick films, and coatings. The water content in a ceramic can be reduced from 25 to 5 vol % within 10–15 minutes, after which drying can be completed using conventional forced air techniques (see INFRARED TECHNOLOGY AND RAMAN SPECTROSCOPY).

Supercritical and Freeze Drying. To eliminate surface tension related drying stresses in fine pore materials such as gels, ware can be heated in an autoclave until the liquid becomes a supercritical fluid, after which drying can be accomplished by isothermal depressurization to remove the fluid (45,69,72) (see SUPERCRITICAL FLUID). In materials that are heat sensitive, the ware can be frozen and the frozen liquid can be removed by sublimation (45,69).

Presinter Thermal Processing

A number of changes can occur on heating a ceramic prior to sintering, including additional drying, burnout of organic additives and impurities, removal of chemically bound water and water of crystallization, and decomposition of inorganic precursors or additives (29). These processes may be accomplished by a separate heat treatment well below the sintering temperature, or in a controlled series of ramps and isothermal holds in a single heat treatment process. For traditional clay ceramics, a separate heat treatment termed a bisque firing is often performed prior to glazing and sintering.

Thermal analysis using differential scanning calorimetry (dsc), thermogravimetric analysis (tga), and differential thermal analysis (dta) can provide useful information about organic burnout, dehydration, and decomposition.

Organic (Binder) Burnout. Organic decomposition (29,42,45,68), which occurs by dissociation or pyrolysis, produces gaseous products that may be hundreds of times the volume of the ceramic part. To preclude the development of catastrophic stresses from gases evolved within the ceramic body, organics must be removed gradually, prior to sintering to high relative density, when the permeability of the body is high. Organics are typically removed at < the sintering temperature. Incomplete binder burnout can result in residual carbonaceous matter in the finished product that can degrade or alter its properties.

Dehydration. Residual liquid and physisorbed moisture on particle surfaces can be eliminated on heating to ~200°C. Temperatures in excess of 1000°C may be required to eliminate chemisorbed water (29). Kaolin must be heated to 700°C to liberate the water of crystallization and produce the desired dehydrated aluminosilicate. As with binder burnout, rapid gas evolution from rapid dehydration can result in catastrophic stress development within a body.

Decomposition. Decomposition (29,68) processes are primarily accomplished in the beneficiation stage of processing by calcination; however, minor concentrations of sintering aids, which may be added as salt precursors, can be decomposed by heating prior to sintering.

Sintering/Thermal Consolidation

Most ceramics are thermally consolidated by a process described as sintering (29,44,68,73–84), in which thermally activated material transport transforms loosely bound particles and whiskers or fibers into a dense, cohesive body.

Sintering. A ceramic densifies during sintering as the porosity or void space between particles is reduced. Additionally, the cohesiveness of the body increases as interparticle contact or grain boundary area increases. Both processes depend on and are controlled by material transport.

Thermodynamic Driving Force for Material Transport. Under the influence of elevated temperature and or pressure, atoms move to lower energy, thermodynamically more stable positions within the system to decrease the volume-free energy of the system. In a powder compact, excess volume-free energy is present primarily in the form of excess pore surface or interfacial energy, ie, liquid–vapor and or solid–vapor interfaces, and the driving force for sintering can be approximated by $dG = -\sum \gamma_i dA_i$, where γ_i is the interfacial energy and A_i is the interfacial area. The interfacial area of a powder compact decreases as material transport occurs during sintering.

The primary driving force for material transport comes from the chemical potential difference that exists between surfaces of dissimilar curvature within the system. The greater the curvature, ie, the finer the particle size, the greater the driving force for material transport and sintering.

Material Transport. During sintering, material transport can occur by solid-state, liquid-phase, and vapor-phase mechanisms individually or in combination. The consequences of material transport during sintering, and the different paths of transport are summarized in the two sphere model shown in Figure 3. Initially during sintering, material is transported from higher energy convex particle surfaces to the lower energy, concave grain boundary pore intersections to form necks between adjacent particles. As sintering progresses, interparticle necks grow, grain boundary area increases, interparticle contacts flatten, and the free energy of the system decreases. Densification occurs in a powder compact as the distance between particle centers and the volume of the compact decreases during sintering.

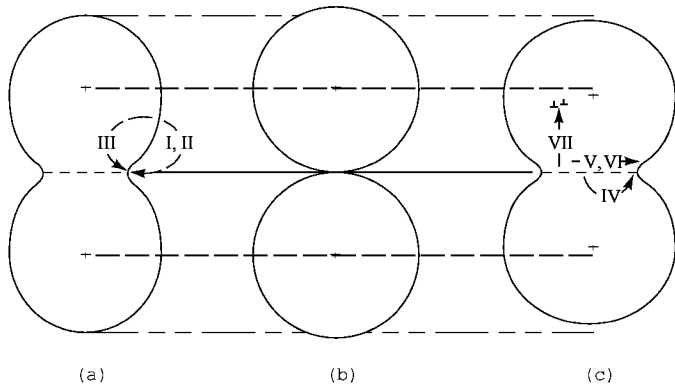


Fig. 3. The two-sphere model illustrating material transport paths I–VII during sintering where (a) represents coarsening; (b), the two spheres before sintering; and (c) densification. The + indicates the center of the sphere.

Material transport can also effect coarsening during sintering. Coarsening is the term used to describe material transport that changes the geometry of the system without resulting in densification, ie, the distance between particle centers remains constant. Coarsening decreases the driving force for material transport without affecting densification, and it is often considered to be an undesirable, competing process. Both densification and coarsening mechanism are generally operative at any given time during sintering.

Densification and Microstructure Development. The microstructure both of a sintered ceramic and development during sintering are also controlled by thermodynamics. The material transport that occurs during sintering manifests itself as grain boundary formation, interparticle pore shrinkage and annihilation, particle compact densification, and grain growth. Initially, interparticle necks and grain boundaries form, creating a three-dimensional array of approximately cylindrical, interconnected, ie, continuous pore channels. These pore channels shrink in diameter during intermediate-stage sintering, and ultimately pinch off to form closed, ie, isolated, approximately spherical pores for final-stage sintering. Additional pore shrinkage and grain growth occur during final-stage sintering.

The primary objective of sintering is to produce a cohesive body of the desired size and shape having a microstructure that optimizes the desired in-use properties. For ceramics, this is usually a theoretically or nearly theoretically dense body comprised of fine (micrometer size), uniform grains.

Physical Characteristics and Property Effects. Powder physical characteristics that can affect sintering include particle size, particle packing, ie, pore size and green density, and particle shape. Particle size has the most pronounced effect on sintering. In general, because material transport occurs faster over shorter distances and less material transport is required to eliminate smaller pores, the finer the particle size, the faster the sintering process, and the lower the sintering temperature. The larger grains grow at the expense of smaller ones, and the smaller pores are preferentially eliminated during sintering. Consequently, as sintering progresses, the average size of the grains and pores in the compact increase and the size distributions become narrower. Densification of large grain and pore size compacts, and compacts comprised of a distribution of grain and pore sizes during sintering, is often limited to <100% theoretical density. Uncontrolled grain growth during final-stage sintering can result in intragranular porosity that also limits densification.

Particle packing may be the single most important physical characteristic of a powder compact. Improved particle packing increases particle coordination and the relative density of the compact, increasing the number of material transport paths for densification, while decreasing the concentration, size, and size distribution of the pores present in the powder compact. Consequently, densification occurs faster, to higher end point densities, and with less overall volume shrinkage during sintering. Uniform particle packing in a green compact ensures uniform densification and shrinkage. Nonuniform particle packing resulting from the presence of agglomerates, ie, densely packed fine particle clusters, or density gradients is undesirable. Ceramic fabrication processes are usually designed and controlled with the intent of optimizing green density while minimizing density gradients during forming.

Particle shape also affects the sintering of a powder compact. Jagged or irregular shaped particles, which have a high surface area to volume ratio, have a higher driving force for densification and sinter faster than equiaxed particles. High aspect ratio platey particles, whiskers, and fibers, which pack poorly, sinter poorly.

Material properties, including surface energy, diffusion coefficients and fluid viscosity, and bond strength are also important factors in sintering. Surface energy anisotropy, which is common in crystalline ceramics, can lead to differential densification, nonuniform and exaggerated grain growth, and end point densities less than theoretical. Bond strength also affects sintering. Strongly bound covalent materials like SiC, Si₃N₄, and BN are typically difficult to sinter without a sintering aid. Weakly bound ionic materials like NaCl are also difficult to sinter because these tend to dissociate during sintering.

Phase transformations can also be an important factor in sintering. Volume changes in materials such as quartz and zirconia from polymorphic phase transformations on heating and cooling can generate catastrophic stresses that can destroy a ceramic body. Damage and loss can be minimized by carefully controlling the cooling rate, or by controlling the size and or concentration of materials that undergo destructive phase transformations during processing. The polymorphic phase transformation in zirconia can be controlled and beneficially utilized to produce toughened ceramics.

Chemical impurities may form a solid solution that alters the rate and or mechanism of material transport, second-phase precipitates that pin grain boundaries and impede grain growth, or a liquid phase that enhances densification relative to coarsening. Minor additions of appropriate impurities can provide improved control over microstructure development during sintering. MgO-doped Al_2O_3 is the classic example in ceramics. Without MgO, the crystalline anisotropy in the Al_2O_3 system favors the formation of large lathlike grains; however, with as little as a few hundred parts per million MgO, fine, equiaxed, Al_2O_3 grains can be sintered to $\sim 100\%$ theoretical density in <1 h at $\sim 1500^\circ\text{C}$. Chemical impurities that are intentionally added to a system to promote sintering and or control grain growth are referred to as dopants or sintering aids.

Sintering Parameters. For a given material system, densification and microstructure development are primarily controlled by the sintering temperature, time, pressure, and atmosphere. Ceramic sintering is a thermally activated process that follows an Arrhenius-type behavior. Consequently, material transport and sintering occur faster at higher temperatures, but so does coarsening. Typically, ceramics are sintered at 0.50–0.75 of the absolute melting temperature.

Time is another important parameter. If the sintering time is short, a low density, porous ceramic body may be obtained. If the sintering time is long, coarsening mechanisms may take over and produce a coarse grained microstructure. Short to intermediate sintering times are used to manufacture fine grain size, high strength ceramics such as alumina cutting tools, whereas longer times are used to manufacture larger grain size, more creep-resistant ceramics such as Si_3N_4 for advanced heat engines. Extended sintering times (>2 h) are used to manufacture large grain size, high permeability ferrites, and high permittivity ferroelectrics.

In contrast to conventional sintering, which is typically conducted at atmospheric pressure or in vacuum, pressure sintering is conducted using an externally applied pressure. The applied pressure enhances the driving force for material transport during sintering, enhancing the rate of densification and making it possible to densify materials that are difficult to densify by conventional sintering. Oxide ceramics are typically sintered in an oxidizing or inert atmosphere to avoid reducing transition metals and degrading the optical properties and or aesthetics of the finished product. Depending on the oxygen partial pressure, lead zirconate titanate (PZT) can be densified by solid-state or liquid-phase sintering mechanisms; however, to optimize its piezoelectric properties, precautions must be taken to maintain a PbO overpressure to limit lead loss and maintain stoichiometry during sintering. Si_3N_4 and AlN are typically sintered in a nitrogen atmosphere to prevent nitrogen dissociation and or oxidation during sintering. SiC must also be sintered in a nonoxidizing atmosphere to avoid oxidation. In processing ferrites (qv), the partial pressure of oxygen must be controlled to optimize magnetic properties. In special cases, such as in processing $\text{YBa}_2\text{Cu}_3\text{O}_7$ ceramic superconductors, it is necessary to control and vary the sintering atmosphere during processing to optimize densification and properties.

Conventional Sintering. Ceramic sintering is usually accomplished by heating a powder compact to ca two-thirds of its melting temperature at ambient pressure and holding for a given time. Densification can occur by solid-state, liquid-phase, or viscous sintering mechanisms.

In solid-state sintering (29,68,78–81) densification occurs by solid-state diffusion-controlled material support. Examples of two technologically important ceramics that density by solid-state sintering are MgO-doped Al_2O_3 and Y_2O_3 -stabilized ZrO_2 .

In general, material transport occurs faster through a liquid than through a solid. Thus densification generally occurs faster in the presence of a liquid phase as compared to solid-state sintering. The presence of a liquid during sintering can also lower the temperature required for densification. For example, polycrystalline alumina, which requires a sintering temperature of $1500\text{--}1600^\circ\text{C}$, can be densified faster and at temperatures hundreds of degrees lower using 0.5–6 wt % of an additive that forms a liquid phase during sintering (29). It is virtually impossible to densify materials such as SiC and Si_3N_4 without a liquid phase. When sintering with a liquid phase, trapped gases in closed pores often impede and limit densification. Additionally, a residual liquid or glass phase at the grain boundaries can degrade the properties of the finished product.

Liquid-phase sintering (LPS) (68,76,78–80,82) involves sintering with a liquid that is persistent throughout the sintering process. LPS is significantly more complex than solid-state sintering as there are more phases, interfaces, and material transport mechanisms to consider. The requirements for LPS are that the liquid wet the solid particles, that there is sufficient liquid present to wet the particles, and that the solid is soluble in the liquid. In general, the rate of densification increases with decreasing viscosity, increasing solubility, and increasing liquid concentration. Temperature is a critical processing parameter in LPS as the viscosity of the liquid decreases and the concentration and reactivity, ie, the solubility of the solid in the liquid, increase dramatically with increasing temperature above the eutectic temperature.

Reactive LPS (68,76,82) is similar to LPS, but differs by the fact that enhanced diffusion through a chemical reaction or phase transformation promotes faster densification. Examples of reactive liquid-phase sintered ceramics include MgO, Y_2O_3 , and or Al_2O_3 doped Si_3N_4 . Transient LPS (76,82) takes advantage of LPS mechanisms and enhances densification in the presence of a liquid during sintering, after which the liquid vaporizes or transforms to a solid solution. Transient LPS produces ceramics devoid of a liquid grain boundary phase; consequently the finished product exhibits improved mechanical properties. LiF-doped MgO is an example of a transient liquid-phase sintered ceramic. Viscous sintering (83), which occurs by surface tension driven viscous flow, is widely used in the processing of glasses and glass-ceramics (qv) for optical and electronic applications. Nonreactive liquid-phase sintering (NLPS) (84) utilizes a combination of LPS and viscous sintering mechanisms to effect densification during sintering. Low temperature sintering ceramic-filled glass, ie, glass matrix, composites for electronic packaging, which typically contain >50 vol % glass, densify by NLPS. Densification and densification rate increase with liquid concentration and temperature during sintering.

Conventional Sintering Equipment. Like drying furnaces, sintering furnaces (29,76,85) can be periodic or continuous in nature. Periodic kilns offer greater flexibility; continuous tunnel kilns are more economical. Advanced ceramics are typically sintered in high purity, controlled atmosphere furnaces by electric resistance heating. Ceramic furnaces used to fire traditional ceramic ware are generally heated with inexpensive natural gas, oil, wood, or coal.

Pressure Sintering. Pressure sintering employs the simultaneous use of pressure and temperature to effect densification during sintering. The externally applied pressure supplements the existing surface tension driving force for material transport during conventional sintering, resulting in an increased driving force and faster densification at the same temperature as conventional sintering, or an equal driving force and densification rate at a lower temperature. Pressure sintering also enhances the rate of densification relative to coarsening, so dense, fine grain size ceramics can be fabricated with little or no sintering aid. The increased driving force for material transport and densification also makes it possible to eliminate larger pores.

Because of higher manufacturing costs relative to conventional sintering, pressure sintering is usually reserved for manufacturing ceramics that are difficult to sinter to high density by conventional sintering, such as nonoxide ceramics, and to produce specialty, pore-free ceramics with improved properties, such as CaF_2 radomes and hard ferrite recording heads.

Hot Pressing. Hot pressing (29,45,68,78–80,86), the oldest and most widely used pressure sintering technique, involves compressing a heated powder in a die between two forming rams. The process is similar to dry pressing, except that the pressing is conducted at the sintering temperature. Hydraulic presses are typically used to apply the pressure, and graphite dies, used to temperatures in excess of 2000°C , but limited to a maximum pressure of ~ 100 MPa, are commonly used.

Graphite powder impurities, metal oxide reduction, pressing gradients, and preferential grain alignment can be problems in hot pressed ceramics. Additionally, hot pressing is limited to forming simple shapes, and considerable machining may be required to produce the desired finished product.

Hot Isostatic Pressing. Hot isostatic pressing (HIP) (45,68,78,87) is similar to cold isostatic pressing used in green forming with the exceptions that pressing is conducted at the sintering temperature, and the pressing medium is typically a gas. Argon or nitrogen gas is generally used, however, helium, oxygen, and mixtures of argon and oxygen have also been used. HIP allows for net and near-net forming without pressing gradients. Complex shape rotor blades and axial rotors have been formed by HIP which can be conducted at temperatures up to 2000°C and ~ 300 MPa (3×10^6 atm). Sintered materials with impermeable surfaces can also be subjected to HIP to higher density, a process that has successfully been used to

produce improved property BaTiO₃, multilayer capacitors and hard ferrites for magnetic recording heads.

Materials to be subjected to HIP must be impermeable to the pressurizing gas. Glasses and refractory metals have been used to "can" ceramics, or ceramics can be presintered to the closed pore stage, ie, >92% theoretical density (TD), to produce an impermeable surface for HIP.

Hot Forging. Hot forging (78) takes advantage of the plastic or plasticlike properties of ultrafine grain crystalline ceramic compacts and crystalline ceramic compacts containing a fluid liquid or viscous glass phase at the sintering temperature. Plasticlike flow by grain boundary sliding under the influence of an applied stress at the sintering temperature results in simultaneous deformation and densification. By controlling deformation with forming dies, net and near-net shapes can be formed.

Novel Sintering Methods. Novel sintering methods employ combinations of radiation and conduction heating to directly heat ceramic parts rapidly in low mass furnaces. Rapid heating often promotes faster densification relative to coarsening, resulting in densification to high relative densities faster, with less grain growth. Additionally, direct sample heating minimizes the energy wasted heating the surrounding furnace and reduces the time required for heating and cooling.

Plasma Sintering. Plasma sintering (88) offers an economical means of rapidly sintering ceramics using rapid heating rates of up to 100°C s to temperatures up to 10,000°C. Sintering times, on the order of tens of seconds, produce up to 99.5% dense, fine grain size microstructures with improved mechanical properties. Rapidly heating, sintering, and cooling by plasma sintering also offers the possibility of producing unique microstructures comprised of metastable phases.

Microwave Sintering. Microwave sintering (89) offers the potential of uniformly processing large volume parts both rapidly and economically. Rapid heating at up to 600°C min to temperatures up to 2000°C can be achieved by microwave heating. Microwave sintering is faster than conventional sintering and may favor densification at lower temperatures.

Rapid Thermal Processing (IR Sintering). Selective and preferential heating using ir radiation provides the potential for faster heating, shorter soak times, and faster cooling. Ir sintering can be 2–3 times faster than conventional sintering, and offers improved control over microstructure development and the benefit of simultaneously processing dissimilar materials.

Chemical Vapor Deposition. Chemical vapor deposition (CVD) (45,68,78,90) is a means of fabricating bulk ceramics, or depositing ceramic coatings (qv) on solid surfaces utilizing a homogeneous or heterogeneous surface vapor chemical reaction. CVD can be used to deposit high purity, fine grain size, controlled morphology ceramic films or monoliths at relatively low temperatures. CVD is used in advanced electronics to form dielectrics in metal oxide semiconductors (MOS), transistors and capacitors, insulators, and diffusion barriers. Additionally, in a process in which a ceramic is deposited on a mandrel, CVD is used to manufacture dense, high purity cubic boron nitride, BN, specialty refractories (qv).

Reaction Formed Ceramics. A variety of specialty ceramics are produced by a combination of a chemical reaction and growth, or by simultaneous chemical reaction and consolidation using relatively novel ceramic reaction forming and thermal consolidation processes. Reaction forming processes provide the potential of producing unique ceramics and ceramic composites and high purity ceramics for specialty applications.

Directed Oxidation of a Molten Metal. Directed oxidation of a molten metal or the Lanxide process (45,68,91) involves the reaction of a molten metal with a gaseous oxidant, eg, Al with O₂ in air, to form a porous three-dimensional oxide that grows outward from the metal ceramic surface. The process proceeds via capillary action as the molten metal wicks into open pore channels in the oxide scale growth. Reinforced ceramic matrix composites can be formed by positioning inert filler materials, eg, fibers, whiskers, and or particulates, in the path of the oxide scale growth. The resultant composite is comprised of both interconnected metal and ceramic. Typically 5–30 vol % metal remains after processing. The composite product maintains many of the desirable properties of a ceramic; however, the presence of the metal serves to increase the fracture toughness of the composite.

Self-Propagating High Temperature Synthesis. Self-propagating high temperature synthesis (SHS) (45,78,92) offers the potential for simultaneous synthesis and densification. Combustion front temperatures range from ~2200–2700° C and the combustion wave propagates at 0.1–100 cm s. Sintered parts tend to be porous; however, higher densities can be achieved by applying pressure during the combustion process or by melt casting. SHS has been used successfully to produce corrosion-resistant coatings on pipes.

Vapor and Reactive Liquid Infiltration. Chemical vapor infiltration (CVI) (45,90,93,94) is a modified version of CVD whereby a matrix is chemically deposited within a porous preform by a solid–vapor chemical reaction. CVI provides a means of making fiber-reinforced ceramic matrix composites without chemically, thermally, or mechanically damaging the fragile fibers. Particulate composites are also formed by CVI which involves vapor-phase mass transport over distances corresponding to the size of the preform. The mass of the preform increases with time as the vapor deposits and reacts on free surfaces within the preform. CVI requires a porous preform and the reaction proceeds until the pore channels plug or close off at ~90% TD and the reacting gas can no longer infiltrate the preform. CVI is a time-intensive process taking days to weeks to complete; however, an extremely high purity, fine grain matrix devoid of sintering aids or residual glassy phases is produced. Products manufactured by CVI include reaction bonded silicon nitride (RBSN) and reaction bonded silicon oxynitride that have good corrosion resistance to fluorides and chlorides. Additional products include carbon and silicon carbide fiber and matrix composites for aerospace applications and heat exchangers (see ABLATIVE MATERIALS; HEAT EXCHANGE TECHNOLOGY).

Reactive liquid infiltration (45,68,90,93,94) is similar to the CVI process used to make RBSN. Driven by capillarity, a reactive liquid infiltrates a porous preform and reacts on free surfaces. Reactive liquid infiltration is used to make reaction bonded silicon carbide (RBSC), which is used in advanced heat engines and as diffusion furnace components for semiconductor wafer processing.

Postsintering Processes

Traditional ceramic processing is generally complete after forming and firing. In contrast, advanced ceramics used in engineering applications may require postsintering processing (95,96). Machining may be required to meet dimensional tolerances and surface finish requirements, thermal annealing may be required to optimize properties, or a surface coating or modification may be required to alter the properties of a ceramic surface for a given application.

Machining. Ceramics can be machined using mechanical, thermal, and chemical action. Techniques employed in machining ceramics include abrasive grinding, chemical polishing, electrical discharge machining, and laser machining (95,96).

Annealing. Oxygen sensitive ceramics often require a postsintering thermal anneal in a controlled partial pressure oxygen atmosphere to achieve the stoichiometry that optimizes properties (76). For example, the magnetic permeability of manganese zinc ferrite, MnO_{0.5}ZnO_{0.5}Fe₂O₄, and the electrical properties of YBa₂Cu₃O₇ ceramic superconductors are strongly dependent on oxygen concentration. Additionally, insulating metal oxides can be reduced in an oxygen deficient atmosphere to become electrical conductors, and electrically conducting metals in metal and ceramic co-fire microelectronic packaging systems can oxidize in an oxygen-rich atmosphere to become electrical insulators during sintering. Sometimes the oxygen partial pressure that favors a high sintered density is different from the one that yields optimum properties. In such cases sintering is initially conducted in one atmosphere and the properties are optimized by subsequently thermal annealing in another.

Surface Coatings. The surface properties and characteristics of a ceramic can be modified with coatings (58,68,78,97). Coatings are applied to traditional clay ware to create a stronger, impermeable surface, and for decoration. Coatings may be applied to advanced structural ceramics and ceramics used in corrosive environments to improve strength, abrasion resistance, ie, wear or erosion, and corrosion resistance. Coatings can be applied dry, as slurries, by spraying, or by vapor deposition.

Glaze coatings (58) are applied to dry or bisque-fired clay ceramics to form a strong, impermeable surface that is aesthetically pleasing. Protective ceramic coatings can also be deposited by CVD (68,90). Plasma activated CVD has been used extensively to produce diamond and diamondlike films. Diamond films can also be used to make optical coatings with a tailored refractive index.

Sol-gel coatings (97,98), which are used to produce reflective, colored, and anti-reflective coatings for glass, can also be used in optoelectronic and integrated optic applications as modulators and switches, eg, sol-gel polycrystalline ferroelectric ceramic films. Sol-gel coatings can also be used to form films of dielectric insulators (qv), high temperature superconductors, capacitors, and piezoelectrics for advanced microelectronic packaging. Common methods of applying sol-gel coatings include dipping and spin coating.

Plasma or flame spray coatings (76,95) are applied like spray glaze coatings except that on passing through the spray gun, the powder feed is superheated by a plasma or flame to produce molten droplets. Upon impinging the object surface, the molten droplets spread to form a continuous coating and are rapidly quenched and solidified. The rapid cooling of the droplets on the ware surface can lead to the formation of nonequilibrium phases with unique properties. Plasma spray coatings are used to form conductive, refractory, and erosion- and corrosion-resistant coatings.

Thin coatings can be formed by ion deposition or sputtering (95), whereby an electron beam strikes a target to produce ions that condense on the object surface. This process is used to alter the electrical properties of a surface by depositing either a conducting or insulating layer. Ion beam deposition is limited to forming thin coatings in a vacuum.

Surface Modification Techniques. Other means of modifying the surface of a ceramic include ion implantation (qv), ion exchange, and quenching. Ion implantation (95) is accomplished by physically bombarding and stuffing the surface of a ceramic with ions. Ion exchange involves the chemical exchange of a larger cation for a smaller one of equal valence in the surface. Thermal quenching by rapid cooling results in differential cooling between the surface and the bulk, freezing in a less ordered, higher volume structure at the surface relative to the bulk such as in tempered glass.

Processing–Microstructure–Properties

The processes employed in manufacturing a ceramic are defined and controlled to produce a product with properties suited to a specific application. Processing–microstructure–property relationships are determined by characterizing the ceramic raw materials, mixes, and the formed ceramic body intermittently during processing and after final thermal consolidation. It is possible to modify and optimize processes to optimize properties and to identify and correct processing deficiencies when less than optimal properties are obtained. Examples of some process–microstructure–property relations in advanced ceramics are outlined in Figure 4.

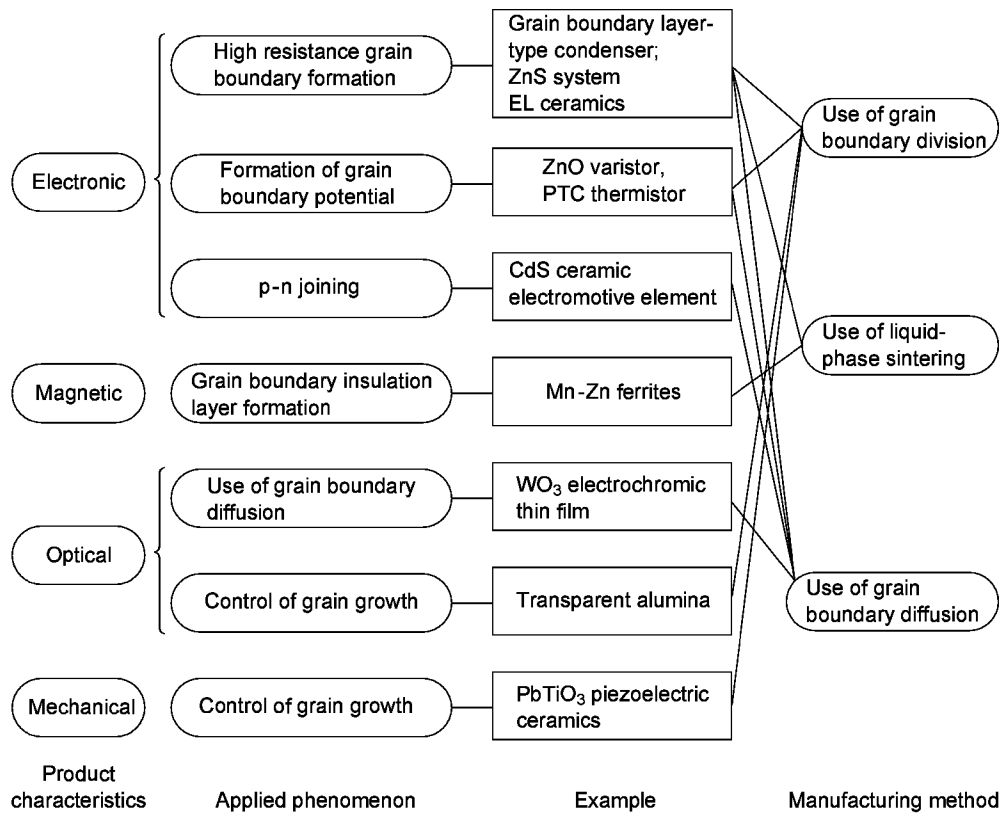


Fig. 4. Process–microstructure–property relationships in advanced ceramics (99).

Characterization. Ceramic bodies are characterized by density, mass, and physical dimensions. Other common techniques employed in characterizing include x-ray diffraction (XRD) and electron or petrographic microscopy to determine crystal species, structure, and size (100). Microscopy (qv) can be used to determine chemical constitution, crystal morphology, and pore size and morphology as well. Mercury porosimetry and gas adsorption are used to characterize pore size, pore size distribution, and surface area (100). A variety of techniques can be employed to characterize bulk chemical composition and the physical characteristics of a powder (100,101).

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Mechanical Properties and Behavior

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Structural ceramics are used in applications such as gas turbines, advanced heat engines, machining, heat exchangers, aerospace components, armor, thermal barrier coatings, and bearings. Advantages of ceramics over metals include dimensional stability; low densities, which translate into weight savings and increased fuel efficiencies; high temperature capabilities; and corrosion resistance. Although metals are ductile, and thus have greater damage tolerance than ceramics, metals are limited to much lower temperatures. For example, the melting points of aluminum and 304 stainless steel are 660°C and from 1400–1450°C, respectively, whereas those of alumina, Al₂O₃, and stabilized zirconia are 2020°C and from 2500–2600°C.

The overriding concern with regard to the mechanical performance of ceramics is their brittleness and hence sensitivity to flaws. There is usually little or no warning that failure is imminent because deformation strain prior to failure is usually less than 0.1%. As a result, a primary thrust of structural ceramics research has been the development of tougher ceramics. Ceramics now exist that have toughness values of 20 MPa·m^{1/2} and strengths that exceed 2000 MPa (3 × 10⁵ psi) (1). These values compare to toughness values of 120–153 MPa·m^{1/2} and strengths of 1380–1790 MPa for structural metals such as AF1410 high strength steel (2) (see also [ADVANCED CERAMICS, STRUCTURAL](#)).

The mechanical properties of ceramics are very sensitive to starting materials, forming processes, heat treatment conditions, and surface preparation. The relations between the structure and mechanical properties of ceramics are particularly strong and complex. Some of the unique aspects are the strong dependence on grain size and the dependence of many properties on extremes rather than averages (3). For example, consider a tensile rod containing a significant volume of pores. If the pores are concentrated in one region of the cross section, this extremely low value of the cross section, not the average value, determines the load-bearing capacity of the body. A comprehensive review is available (3).

Properties and Behavior

Elastic Behavior. Elastic deformation is defined as the reversible deformation that occurs when a load is applied. Most ceramics deform in a linear elastic fashion, ie, the amount of reversible deformation is a linear function of the applied stress up to a certain stress level. If the applied stress is increased any further the ceramic fractures catastrophically. This is in contrast to most metals which initially deform elastically and then begin to deform plastically. Plastic deformation allows stresses to be dissipated rather than building to the point where bonds break irreversibly.

Elastic behavior is commonly quantified by the Young's modulus *E*, the proportionality constant between the applied tensile stress σ, and the tensile strain (Δ length / original length).

$$\sigma = E\epsilon$$

(1)

Materials having high elastic moduli deform less for a given stress. Typical *E* values are shown in Table 1.

Table 1. Properties of Ceramics and Other Materials

Material	Young's modulus, GPa ^a	Poisson's ratio
soft rubber	0.007–0.07	0.49
nylon	2.8	0.40
ice	9	0.2–0.88 ^b
concrete	14	0.20
aluminum	70	0.34
plate glass	70	0.27
copper	110	0.34
ZrO ₂ , partially stabilized	205	0.23
Al ₂ O ₃	380	0.26
SiC	207–483	0.14
diamond	1050	0.20

^a To convert GPa to psi, multiply by 145 × 10³.
^b Values for the Poisson's ratio of ice are highly dependent on composition, structure, and strain rate (4).

Because the ease with which atoms can be separated depends on bond strength, the materials having the strongest bonds and highest bond densities have the highest Young's modulus. Crystals are often anisotropic because bond strengths and density are a function of direction. In single crystals this leads to anisotropy in the elastic moduli such that the strain depends on the stress application direction. Most polycrystalline materials are isotropic because the anisotropies of individual grains (single crystals) average out to zero over all the grains. Glasses are elastically isotropic because of a random network structure.

Another commonly used elastic constant is the Poisson's ratio ν, which relates the lateral contraction to longitudinal extension in uniaxial tension. Typical Poisson's ratios are also given in Table 1. Other less commonly used elastic moduli include the shear modulus *G*, which describes the amount of strain induced by a shear stress, and the bulk modulus *K*, which is a proportionality constant between hydrostatic pressure and the negative of the volume change (−Δ*V* / *V*).

Porosity has a significant effect on elastic moduli. Empirical relations of the form

$$E = E_o e^{-bP}$$

(2)

where *E_o* = Young's modulus of dense material, *P* = relative volume of porosity, and *b* = constant, generally describe the elastic behavior of ceramics. Microcracks decrease the elastic modulus because cracked regions deform more easily. Grain size has no effect on the modulus unless the material is very anisotropic and contains large grains that microcrack spontaneously.

Young's modulus can be determined by measuring the stress–strain response (static modulus), by measuring the resonant frequency of the body

(resonant modulus), or by measuring the velocity of sound through the material (sonic modulus).

Strength.

Measured Strength versus Theoretical Strength. Measured strengths of ceramics depend both on the types of flaws that are present and how the strength is measured. The elastic modulus describes how easily atoms in a solid can be moved together or apart for small deformations. If deformations are continued, eventually an atom spacing is reached beyond which there is not enough atomic attraction to hold the atoms together. If entire planes of atoms separate, the ceramic breaks and its theoretical tensile strength has been reached. The theoretical tensile strength of the material, σ_{theor} , has been approximated by

$$\sigma_{\text{theor}} = \left(\frac{E\gamma}{a}\right)^{1/2} \approx \frac{E}{10}$$

(3)

where a = equilibrium spacing between planes of atoms, γ = fracture surface energy, and E = Young's modulus (5).

If all bonds in a material were stressed equally up to the point of failure, the strength of a ceramic would be the theoretical strength. Large discrepancies between the theoretical and measured tensile strengths of ceramics result from the presence of microstructural imperfections. These imperfections or flaws can raise the local stress to the point that bonds in the immediate vicinity of the flaw can fail a few at a time, as opposed to every atom in the plane failing simultaneously. Regardless of the shape or orientation of a flaw, the energy required to break bonds in a given material is generally constant.

A flaw such as a simple spherical pore concentrates the stress on the bonds in the vicinity of the pore by a factor of two over the applied stress (6); however, most ceramics contain imperfections that enhance the stress to a much greater degree, leading to severe strength reductions. A typical ceramic such as alumina is as much as one hundred times weaker than the theoretical strength.

Stress concentration, such that the crack tip stress exceeds a material's theoretical strength, is a necessary condition for fracture; however, an energy requirement must also be satisfied. It has been recognized that crack growth could only occur if the total energy of the system was lowered by crack growth (7). The energy requirements for crack growth have been postulated to be equal to the energy required to create two new surfaces. Thus

$$\sigma_{\text{fracture}} = \left(\frac{2E\gamma}{\pi c}\right)^{1/2}$$

(4)

where $2c$ = crack dimension. The details of this formulation along with extensive information about brittle fracture is available (7).

A more practical approach for quantifying the conditions required for fracture uses a stress intensity criterion instead of an energy criterion. Using linear elastic theory, it has been shown that under an applied stress, σ_{applied} , when the stress intensity K ,

$$K = \sigma_{\text{applied}} Y(c)^{1/2}$$

(5)

where Y = flaw and loading geometry factor (8), reached a critical value known as the fracture toughness, K_{IC} , fracture would occur. The applied stress required to cause fracture, σ_{fracture} , can therefore be written as

$$\sigma_{\text{fracture}} = \frac{K_{\text{IC}}}{Y(c)^{1/2}}$$

(6)

Ceramic strength is typically measured as a bending, also known as flexural, strength because of the difficulties of gripping ceramic samples and achieving pure tension in tensile tests. If a tensile ceramic specimen is improperly aligned, it experiences shear and bending components and the strength value obtained is invalid. Guidelines for conducting strength tests are available (9). Measured strengths of ceramics are shown in Table 2.

Table 2. Measured Strengths of Common Ceramics

Material	Tensile strength			Compressive strength	
	Measurement technique ^a	Value, MPa ^b	Reference	Value, MPa ^b	Reference
glass					
soda-lime silica (SLS) glass	ROR	79	10		
chemically strengthened SLS glass	ROR	293	10		
Si ₃ N ₄	FP	250	11	3450	12
SiC	FP	345	13	3680	14
Al ₂ O ₃	FP	370	11	4480	12
SiAlON	FP	450	15		
SiC reinforced Al ₂ O ₃ composite ^c	FP	640	16		
Y-TZP ^d	TT	745	17		
	FP	1630	17		
ZrO ₂ , CaO stabilized				2000	12
Al ₂ O ₃ -ZrO ₂ composite	TP	2400	1		

^a ROR = ring-on-ring bending; FP = four-point bending; TT = tensile test; and TP = three-point bending.

^b To convert MPa to psi, multiply by 145.

^c Whisker reinforced SiC, 30 vol %.

^d 2 mol % yttria stabilized tetragonal zirconia polycrystal.

Flaws. Pristine, undamaged ceramics exhibit strengths close to theoretical levels. Strengths of most ceramics, however, seldom approach theoretical levels because of processing flaws and damage introduced by handling, and during service. Examples of flaws commonly found in ceramics are shown in Figure 1.

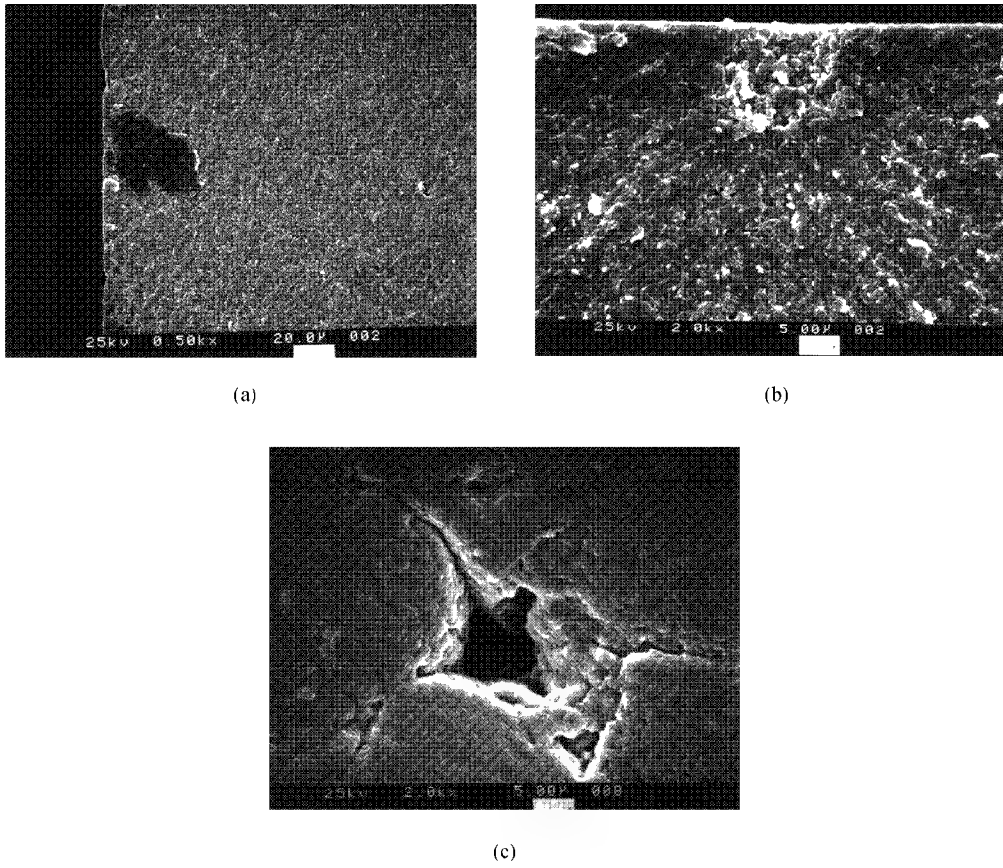


Fig. 1. Strength-reducing flaws commonly found in ceramics: (a) large grain surrounded by fine-grain matrix; (b) porous region resulting from incomplete densification; and (c) pore from where hard powder agglomerates did not sinter together.

Although each ceramic has a characteristic theoretical strength, the fracture toughness K_{IC} and the most severe flaw, ie, the flaw that gives rise to the largest stress concentration, normally determine the actual strength. The larger the flaw, the greater the reduction in strength, and flaws in close proximity may act as a single, more severe flaw.

Microstructural effects on strength, such as porosity, impurities, grain size, and surface condition, are difficult to isolate because frequently several effects occur simultaneously. Strength can be related to porosity using the same general relationship used for elastic behavior (eq. 2), but this model only considers the average porosity, whereas the extremes, such as the largest pore, must be considered (3). A common assumption for the relationship between strength and grain size is that flaw size scales directly with grain size and hence the strength and grain size are related in a similar manner to strength and flaw size (eq. 6). A second relation between strength σ , and grain size G , known as the Hall-Petch relation, is based on microplastic failure mechanisms such as slip, and follows the general form:

$$\sigma = \sigma_c + \frac{1}{BG^{1/2}} \tag{7}$$

where σ_c = resistance to dislocation glide and B is a constant. Equation 7 does not usually describe the observed tensile strength of ceramics at low temperatures because slip is generally not observed in ceramics except at high temperatures or under large compressive stresses. The relation between strength and the presence of impurities depends on the location and form of the impurities, and the failure mechanism. If impurities are present as discrete second phases, they can serve as obstacles to crack propagation; however, they can also act as stress concentrators, or as weak grain boundary fracture paths. Another important effect of impurities on strength is related to the effect on the microstructure, for example the grain size and porosity.

Statistical Variation in Strength. The wide variety of flaw types and sizes in ceramics produces the large (typically $\pm 25\%$) variability in strength that has been one of the principal hurdles to the incorporation of ceramics in structural applications (18). This compares unfavorably with the few percent for variability of the yield stress of a metal. The probability of failure of a ceramic body at a given load depends on the probability of a flaw of a critical size being present in a location where the flaw produces a stress concentration. Some of the strength variability can be attributed to inconsistencies in testing procedures; however, tests performed in accordance with recommended standards can give accurate and consistent results (11).

Many distribution functions can be applied to strength data of ceramics but the function that has been most widely applied is the Weibull function, which is based on the concept of failure at the weakest link in a body under simple tension. A normal distribution is inappropriate for ceramic strengths because extreme values of the flaw distribution, not the central tendency of the flaw distribution, determine the strength. One implication of Weibull statistics is that large bodies are weaker than small bodies because the number of flaws a body contains is proportional to its volume.

The Weibull distribution function expresses the failure probability F as a function of the applied stress σ , and three Weibull parameters σ_μ , σ_o and m

$$F = 1 - \exp \left[- \int_V \left(\frac{\sigma - \sigma_\mu}{\sigma_o} \right)^m dV \right] \tag{8}$$

where σ_μ = the threshold stress below which failure does not occur, ie, where $F = 0$; σ_o = a characteristic strength; V = specimen volume, and m = a measure of the data scatter which is called the Weibull modulus.

A conservative assumption is that σ_μ can be set equal to zero. When the stress σ equals the characteristic strength σ_o the failure probability is 63.2%. Under conditions other than tensile loading, the stress distribution in a body is inhomogeneous. To account for this, a loading factor k is used to calculate the effective volume under stress and kV replaces V .

To obtain the Weibull parameters, the strengths of $n > 30$ samples are measured and ranked from lowest to highest. The probability of failure is then calculated using an estimator:

$$F = \frac{n}{N + 1} \tag{9}$$

where N = number of specimens and n = rank of sample. The data is plotted as $\ln \ln [1 / (1 - F)]$ versus $\ln \sigma$ according to equation 10, derived from

equation 8.

$$\ln \ln \left(\frac{1}{1-F} \right) = \ln V - m \ln \sigma_o + m \ln \sigma$$

(10)

The term V is replaced by kV for any test other than a tensile test.

The terms V (or kV) and σ_o are usually grouped together as a single term; σ_o' and m and σ_o' can be gotten from the slope and intercept, respectively. Typical m values for ceramics range between five and twenty (18); five indicates a high variability in the strength and twenty a relatively low strength variability.

Compressive Strength. Ceramics are much stronger in compression than in tension and are frequently used in applications where they bear compressive loads. Under excessive compressive loads ceramics fail in a brittle manner just as they do in tension; however, the predicted stresses are eight times the predicted tensile stresses (12). In compression, the failure process appears to begin with microplastic deformation, not the growth of pre-existing flaws. Measured compressive strengths are often far below predicted values because of flaws, twinning, improper loading, and internal stresses resulting from effects such as grain anisotropy (12). Measured compressive strengths are shown in Table 2. Although there is limited data relating microstructure to compressive strength, compressive strength appears to be related to grain size via equation 7. Porosity effects have been modeled using the same relation used for Young's modulus and tensile strength (eq. 2).

Fracture Toughness. The fracture criterion was defined by a critical value of the crack tip stress intensity, known as the fracture toughness, K_{IC} . Ceramics often fail in pure tension, designated mode I, and K_{IC} replaces K_C in equation 6. Thus σ_{fracture} , the applied tensile stress at which fracture occurs, is a function of the flaw size and K_{IC} . In all cases the body fails when the local stress concentration at the crack tip reaches the critical value required for bond breakage. Thus the critical stress intensity, K_{IC} , required for bond rupture is considered to be a material constant.

Under some circumstances the crack tip stress intensity is different than far-field stresses would indicate because of microstructural effects behind the crack tip, such as fibers, whiskers, and bridging grains. Often far-field values indicate the crack is propagating at a stress intensity value higher than K_{IC} and this apparent value usually increases as crack length increases. In spite of indications to the contrary, bonds continue to break at the same value of the stress intensity; however, the crack tip is being shielded from some of the applied stress intensity. To minimize confusion about K_{IC} it has been suggested that the farfield value of the stress intensity be called K_{applied} . When there are no microstructural features that effectively reduce the crack tip stress intensity, such as in glasses, the crack tip stress intensity is accurately represented by the far-field values, and K_{applied} equals K_{IC} . In this case, equation 6 can be used to predict what size flaw a material can tolerate at a given stress level.

K_{IC} measurements can be made by introducing a crack of a known size in body having a specific geometry and then loading the body until catastrophic failure occurs. The shape factor Y used to account for different flaw and loading geometries can be found in reference handbooks (8). An alternative approach for determining K_{IC} consists of measuring surface cracks introduced using a sharp indenter (19,20). The low fracture toughness, in units of $\text{MPa}\cdot\text{m}^{1/2}$, of ceramics is demonstrated by values of 2.7–4.2 for alumina, 4–6 for Si_3N_4 , and 8–9 for partially stabilized ZrO_2 , as compared to 0.75 for Pyrex glass, 0.5–1 for common woods parallel to grains, and 3 for nylon on the one end, and 11–13 for common woods perpendicular to grains, 6–20 for cast iron, 30 for silicon carbide reinforced glass, 46 for tool steel, 120–153 for AF1410 high strength steel, and 100–350 for pure ductile metals, eg, Cu, Ni, and Ag (19,20).

R-Curve Behavior. Ceramic toughening efforts have focused on the property of some ceramics to exhibit increased apparent fracture toughness as cracks grow. This increase is seen in terms of the far-field value of the stress intensity required to propagate the crack. An important consequence of this effect, which is commonly referred to as R-curve or T-curve behavior, is that the material has increased damage tolerance because there is a crack size regime in which the strength is independent of the crack size. The underlying basis of R-curve behavior is that the crack tip stress is redistributed, either to immediately adjoining material, as in the case of the process zone formed in transformation toughened materials, or to regions far removed from the crack tip, as in the case of fiber-reinforced ceramics. One reason for the interest in crack interface bridging mechanisms is that this toughening mechanism should operate over a broad range of temperatures. Characteristics of R-curve mechanisms are that they are activated only as the crack advances, the number of activated elements increases as the crack grows, and the measured fracture toughness saturates when the generation rate of shielding elements equals the rate at which elements become inactive.

One implication of R-curve behavior is that the measured fracture toughness is not a material constant equal to K_{IC} ; rather it is a function of the crack length. The material can still be considered to have a constant toughness. However, there are microstructural influences that affect the effective stress intensity K at the crack tip (21). R-curves appear to depend on crack size, microstructure, loading conditions, and component geometry (22). In alumina, where R-curve behavior arises because of ligamentary bridges formed by grains behind the crack tip, grain size determines the scale of grain pullout for grains that bridge the interface (23). At small grain sizes the bridging effect appears to be insignificant. Other microstructural effects include grain boundary toughness, thermal expansion anisotropy, and grain texture, ie, elongated grains.

Transformation Toughening. Transformation toughened materials exhibit enhanced toughness because of an energy-consuming phase transition that occurs when material in the vicinity of a crack is stressed. Because energy is consumed in the phase transformation, the energy available for crack propagation is reduced. The zone containing transformed particles is known as the transformation or process zone. Significant toughening cannot occur until this zone has grown sufficiently to extend behind an advancing crack tip as shown in Figure 2. A comprehensive review of transformation toughening of ceramics is provided (24).

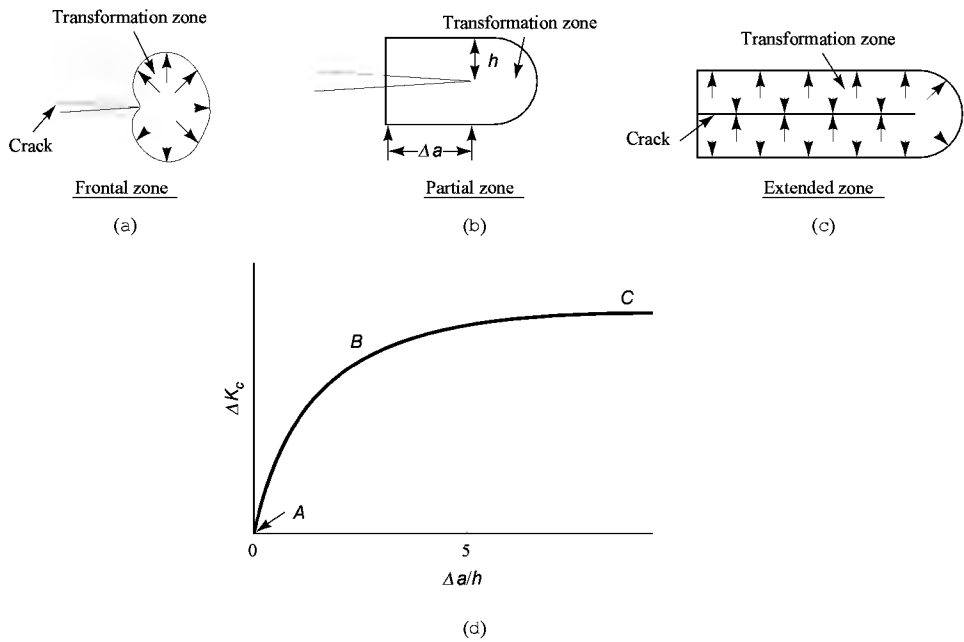


Fig. 2. A schematic of a zirconia body containing a propagating crack: (a) the frontal zone of the transformed material; (b) the partial zone defining Δa and b ; (c) the extended and the transformation and extended zones; and (d) change in fracture toughness as a function of growth of the transformation zone, where A represents the frontal zone; B , the partial zone; and C , the extended zone.

The transformation toughening mechanism has been most successfully exploited in ZrO_2 materials where the phase transformation of interest is from tetragonal to monoclinic ZrO_2 . Microcracking may also play a role in the transformation toughening of ZrO_2 materials because of the extra energy required to produce additional fracture surface. Toughness enhancements of almost 100% (from 5.2–9.5 $\text{MPa}\cdot\text{m}^{1/2}$) have been achieved in ceramics such as Al_2O_3 by adding ZrO_2 as a second phase (24).

Oxides such as CaO , MgO , and Y_2O_3 are added to ZrO_2 to stabilize the tetragonal phase at temperatures below the tetragonal to monoclinic phase-transition temperature. Without stabilizer, the phase transition occurs spontaneously at temperatures below 850–1000°C, and no fracture toughness enhancement occurs (25).

Toughening Mechanisms in Composite Ceramics. Significant toughening has been achieved by fabricating whisker- and fiber-reinforced ceramic composites, and metal–ceramic composites (see COMPOSITE MATERIALS). Toughening primarily results from crack bridging and or crack deflection, both of which reduce the crack tip stress intensity. Crack deflection, which occurs when the reinforcement debonds from the matrix, changes the orientation of the crack relative to the stress application direction, changing the stress distribution around the crack such that the stress intensity at the crack tip bonds is reduced. When a reinforcement phase bridges the crack behind the crack tip, it supports some of the applied load, and therefore shields the crack tip from some of the applied stress intensity. Crack tip shielding gives rise to R-curve behavior and the ability of these materials to resist catastrophic failure as shown in Figure 3.

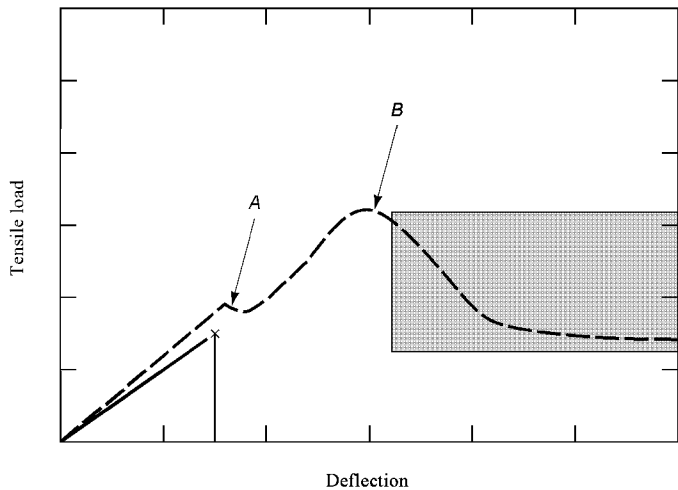


Fig. 3. Tensile stress–strain curve for (---) reinforced ceramic and (—) fiber-reinforced ceramic composite. A represents the point where the matrix begins to crack; B, where the reinforcement begins to fail and the section ■ where reinforcement pulls out of the matrix. X indicates the point of catastrophic failure.

Crack deflection toughening resulting from debonding along interfaces between the matrix and reinforcement phase has been covered extensively in the literature (26–28). Crack bridging, which plays the largest role in enhancing the toughness, depends on intact whiskers or fibers being able to pull out of the matrix behind the crack tip. A very large amount of energy can be consumed in this process that would otherwise be used to propagate the crack. The stress–strain behavior of a fiber-reinforced composite in Figure 3 shows that during the initial stages of loading, the composite exhibits the same behavior as an unreinforced matrix, ie, it is linear elastic. At point A the matrix begins to crack and the slope of the stress–strain curve begins to decrease. At point B the fibers begin to fail and the load the body can support diminishes. The area under the stress–strain curve, past the point where the matrix begins to crack, represents the energy absorbed during fiber debonding and pull-out. Many composites exhibit very large strains to failure and retain some load-bearing capability even after the integrity of the matrix has been lost.

Whiskers or fibers must be able to debond and slide out of the matrix in order for significant toughening to occur. Thus the parameters controlling the toughness of a composite are the interfacial strength and the interfacial frictional stress, τ , which has to be overcome before the reinforcement slides out of the matrix. If the interfacial strength is too high, no debonding occurs and the value of the frictional stress is irrelevant. Methods for controlling the interfacial strength include choosing reinforcement and matrix materials that do not react, and coating the fiber with nonreactive or low strength porous coatings (29). If τ is too large there will be no toughening because the fiber will break rather than pull out. Low τ values produce the greatest toughening with respect to fiber pullout.

Composites have also been made where strengthening is the goal. A high pullout stress, τ , is one of the important parameters for higher strength because high values allow load transfer from the matrix to the high strength fibers. The effect of the sliding stress, τ , on the toughness and strength, highlights the importance of the design of the reinforcement–matrix interface in the overall design of composites. The role of the interface is covered (30).

Metal–ceramic composites, including those made by *in situ* oxidation of infiltrated molten metal known as the Lanxide process (31), have high toughness values that result from residual ductile metal that bridges the crack behind the crack tip (32). Because of the large amount of plastic work required to cause these elements to fail, there is an increase in the amount of energy, or applied stress intensity, required to propagate a crack through the composite. Composites of this type exhibit fracture toughness values as great as three times the matrix toughness (33).

Ferroelasticity. Ferroelastic materials contain domains that can be switched by an applied stress (34) in a manner analogous to magnetic domain switching in ferromagnetic materials. A hysteresis loop between the applied field or stress and the induced state, and a permanent induced state when the applied field is removed, are characteristic of domain switching for both of these properties. The permanent state of a ferroelastic is the permanent strain induced by the applied stress. Many ceramics that exhibit ferroelasticity also exhibit ferromagnetism and or ferroelectricity, such as BaTiO_3 and lead zirconate titanate (PZT). Toughening occurs because energy is absorbed in the switching of the domains. Ferroelasticity has been identified as a source of toughening.

Tetragonal zirconia is a structural ceramic that exhibits ferroelasticity and the toughness enhancement has been estimated to be as high as 5 $\text{MPa}\cdot\text{m}^{1/2}$. An example of a partial hysteresis loop for this material is shown in Figure 4 (35). Domains do not have to be present prior to the stress application because stresses can also nucleate domains (36). Domain nucleation and additional fracture surface generated by fracture along domain boundaries appear to contribute to the toughening.

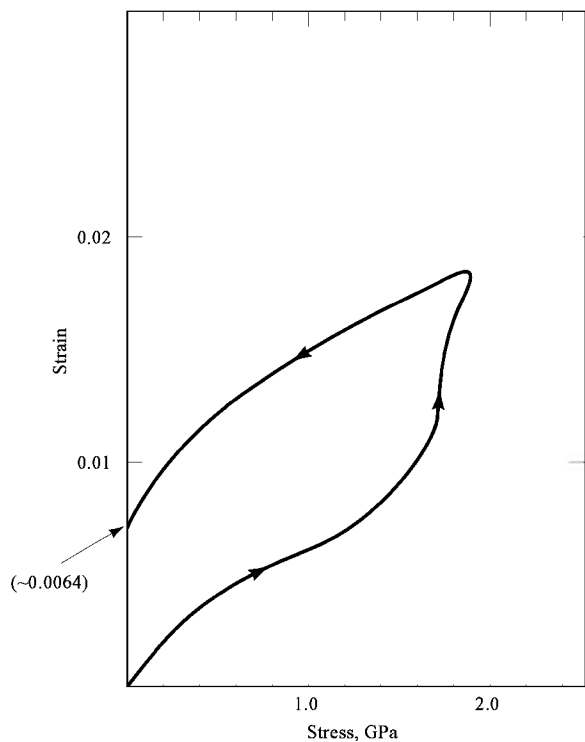


Fig. 4. Partial hysteresis loop for a ferroelastic material. After the applied stress is removed a permanent strain ~ 0.0064 remains (see eq. 1).

Plasticity. Although even at elevated temperatures mechanical failure of ceramics is dominated by brittle fracture, plastic deformation mechanisms often precede brittle fracture. Plastic deformation is also important because of the role it plays in net shape forming operations such as extrusion, which require extremely high strain rates in a deformation regime known as superplasticity (37). At low and high temperatures plastic deformation of crystalline ceramics can occur by slip, but it is not usually observed, except under special conditions, because the required stress levels are usually much higher than those required for brittle fracture. At elevated temperatures plastic deformation can also occur by grain boundary sliding and softening of secondary phases such as glass.

Plastic deformation by slip involves one atom plane sliding past another, or twinning by homogeneous shearing. Once slip occurs there is permanent deformation of the material. Because the stresses required to slide perfect planes of atoms past each other are extremely large, some kind of defect that allows this motion to occur at much lower stress levels must be present. The primary mechanism of slip at relatively low stresses in polycrystalline materials is the motion or glide of line defects called dislocations. Dislocation motion allows bonds to break at relatively low applied stresses because dislocation motion occurs by sequential bond breakage. This is somewhat analogous to fracture. The primary difference between dislocation motion and fracture is that bonds immediately reform after a dislocation has passed, whereas they remain ruptured after a crack front passes.

Slip usually occurs on the planes that have the highest atom density and are the greatest distance from adjacent planes. Therefore the slip systems that can be activated in a crystal depend primarily on crystal structure, and those crystals with the highest symmetry, eg, cubic, have the most available slip systems. Slip systems and the temperatures at which they are activated are available (18).

If a ceramic single crystal is suitably oriented with respect to the applied stress direction, deformation can occur through dislocation motion. The rate of plastic deformation depends on the number of dislocations and their velocity. Although suitably oriented ceramic single crystals such as MgO deform plastically at low temperatures by slip, polycrystalline forms of the same material act in a brittle manner because of geometrical constraints. Plastic deformation in ceramics by slip is also suppressed by the large amount of energy required to move dislocations, especially for covalently bonded ceramics such as SiC and Si₃N₄. As temperature increases, plastic deformation by slip becomes easier because of the increased amount of energy available for dislocation glide. Other plasticity mechanisms also become activated at elevated temperature but in spite of the increased plasticity at these temperatures, failure ultimately occurs in a brittle manner when cracks nucleate at grain boundaries. The total strain in a tensile test prior to fracture is usually less than 1%.

The processes leading up to failure at elevated temperatures are known as creep. Figure 5 shows a typical creep curve divided into four regions. The first region, often ignored, represents the instantaneous deformation that occurs when a load is applied. The second region usually consists of an area of decreasing creep rate and is known as primary or transient creep. The third region, known as steady-state or secondary creep, is the most important for lifetime predictions. In tensile creep tests fracture often occurs in this region. The fourth region is known as tertiary creep and in this region the deformation rate accelerates just prior to complete failure. Fracture occurs as various types of creep damage accumulate. Damage includes loss of internal section from the formation of pores or cavities, linking of the cavities to form cracks, and environmental degradation of the microstructure. Increased temperature or stress increases the creep rate and reduces the time to failure.

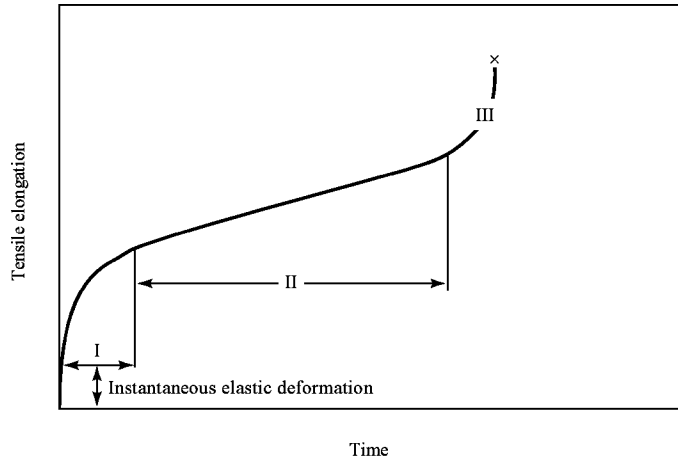


Fig. 5. Tensile elongation vs time demonstrating creep behavior of ceramics. Section I is primary creep; II, secondary or steady-state creep; III, tertiary creep; and X, fracture.

In polycrystalline ceramics, in which creep occurs by dislocation motions controlled by the rate of diffusion of atoms through the lattice, a lattice creep mechanism is said to operate. Far more common to polycrystalline ceramics is diffusional creep, in which deformation occurs by diffusional flow of atoms to and from grain boundaries, either by diffusion through the lattice (Nabarro-Herring creep), or along the grain boundaries (Coble creep) (38,39). Creep can also occur by grain boundary sliding in materials with and without liquid grain boundary phases. Diffusional creep and creep by grain boundary sliding are categorized as boundary creep mechanisms. Detailed information on creep mechanisms can be found in the literature (38,40).

In the steady-state creep regime of ceramics, almost all creep mechanisms fit a strain rate dependence of the form (18):

$$\dot{\epsilon} = \frac{A^* D G b}{k T} \left(\frac{b}{l_g} \right)^{m^*} \left(\frac{\sigma}{G} \right)^{n^*}$$

(11)

where $\dot{\epsilon}$ = strain rate; A^* = dimensionless constant; D = diffusion coefficient (exponential temperature dependence); G = shear modulus; b = Burgers' vector; k = Boltzmann's constant; T = temperature; l_g = grain size; σ = applied stress; n^* = stress exponent which commonly has values of 1–5; and m^* = grain size exponent which commonly has values of 0–3. Analysis of creep data using equation 11 usually allows a specific creep mechanism to be identified, based on the stress and grain size exponent. Once the creep mechanism has been identified the kinetics of crack growth can be identified and lifetime predictions can be made. Creep in some ceramics is sufficiently well understood over a broad range of conditions that the deformation behavior and theoretically predicted behavior can be displayed on maps known as Ashby plots (41). Equation 11 shows that a larger grain size favors increased creep resistance. The potential detrimental effects of second phases are an important consideration for ceramics which require dopants as sintering aids. Impurities affect the diffusion coefficient and may end up as grain boundary phases which are often glassy in nature.

Plastic deformation is commonly measured by measuring the strain as a function of time at a constant load and temperature. The data is usually plotted as strain versus time. Deformation strain can be measured under many possible loading configurations. Because of problems associated with the preparation and gripping of tensile specimens, plastic deformation data are often collected using bend and compression tests.

Hardness. Hardness (qv) is a measure of the resistance of a material to deformation, in particular the resistance to plastic deformation during surface penetration. Hardness is also related to the bond strength. Because covalent and multivalent ionic bonds are strong and highly directional in nature, slip is very difficult in these cases, and ceramics containing these bonds are generally the hardest materials (42). The ratio of the distance between planes of atoms a and the spacing of the atoms in the plane b also plays an important role in how easily planes of atoms slide past each other, and hence in the hardness. Small a/b ratios tend to give harder materials (5). Glasses, in spite of the fact that they are largely covalent and do not contain mobile dislocations, are softer than crystalline ceramics because the bond densities and bond strengths are lower than in polycrystalline ceramics.

Hardness is determined by measuring the penetration (depth or area) when a harder material, such as diamond, is pushed into the surface of the material of interest under a specified load. True hardness is defined as the force divided by the projected area. Vickers hardness tests, which employ a pyramid-shaped indenter, are frequently used to characterize ceramics; however, Vickers hardness calculations normally employ total surface area rather than projected area (43). Measurements are made on the diamond impression shown in Figure 6. Vickers hardness is calculated using

$$H_{V, \text{ total area}} = \frac{0.46 P}{a^2}$$

(12)

where P = indentation load and a = half-length of Vickers impression diagonal. Hardness is normally expressed in units of GPa but Vickers hardness numbers are also expressed in units of kg mm². Many other hardness scales are used; however, conversions between scales is not always possible (44). Hardness values for diamond and some ceramics include:

Material	Hardness, GPa
glass ceramics	6–7
zirconia (partially stabilized)	10–11
silicon nitride	8–19
alumina	18–23
silicon carbide	20–30
diamond	98

Hardness for lead, copper, steel, and cast iron are 0.07, 0.86, 2.23, and from 1–7 GPa, respectively.

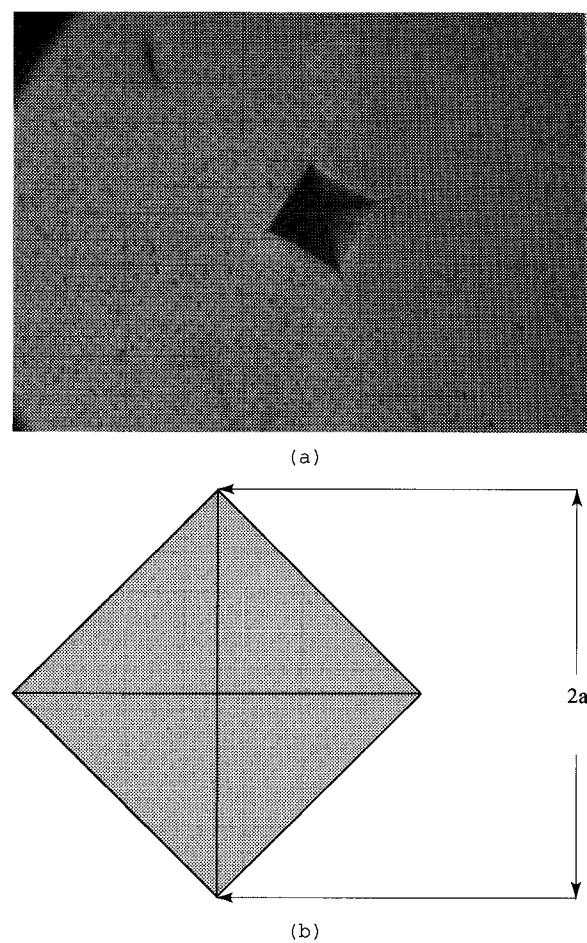


Fig. 6. (a) Vickers indentation in zirconia at 200 X. (b) Schematic of a Vickers indentation showing the dimension used in Vickers hardness determinations.

Hardness decreases with increasing porosity and increased grain size. Solid solution impurities influence hardness, but it is often hard to separate the effect of the impurity on the hardness, from the effect of the impurity on other microstructural effects that influence hardness such as grain size. Further information on hardness of ceramics is available (45).

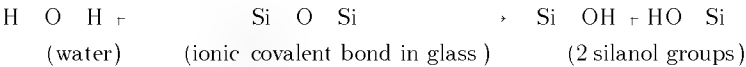
Ceramics deform plastically more readily at higher temperatures and therefore hardness decreases with increasing temperature according to

$$H = H_o \left(1 - \frac{T}{T_o} \right) \tag{13}$$

where H_o = hardness at 0 K and T_o = temperature in Kelvin at which hardness goes to zero (46).

Subcritical Crack Growth. Under most environmental conditions, the strength of ceramics, especially glasses, degrades with time. This phenomenon, known as subcritical crack growth (SCG), stress corrosion cracking (SCC), static fatigue, or delayed failure, involves the slow growth of a pre-existing crack at an applied stress intensity lower than that necessary, ie, the critical value, to propagate a crack without environmental influences. Subcritical crack growth is pernicious because a flaw grows slowly at stresses far below the expected failure load until the flaw is large enough to satisfy the Griffith criterion, and then failure occurs catastrophically.

The mechanism of subcritical crack growth is the reaction of the corrosive medium with highly stressed bonds at the crack tip. In silica, in the absence of stressed bonds, the rate of the reaction between the bonds and corrosive media such as water is very low. The introduction of strain energy into crack tip bonds increases the activity of the bond. For silica glass in water, attack and bond breakage occurs by the following reaction (47):



in which weak bonds between silanol groups replace strong silicon–oxygen bonds. Similar reactions occur with ammonia, methanol, and other liquids (48).

Crack velocity v , as a function of applied K_I , is usually divided into three regions as shown in Figure 7. In region I, v exhibits a power law dependence on K_I . The stress intensity determines the bond reactivity and therefore the rate of bond breakage, the kinetics of the chemical reaction at the crack tip. An increase in the reactive species concentration, eg, water, and increased temperature shift region I to lower K_I . Region II is determined by the rate at which the chemical species travels to the crack tip, and is insensitive to K_I . The plateau velocity depends on the environment. For example, increasing relative humidity raises the plateau. In Region III, v is a strong function of K_I and believed to be independent of environment. Crack velocity in regions I and III can be approximated by an empirical relationship of the form

$$v = AK_I^n \tag{14}$$

where A = material constant and n = subcritical crack growth susceptibility constant. The relationship in equation 14 is most useful for region I because this represents the majority of the component lifetime. At K_{IC} , bonds break without environmental assistance and the crack becomes critical. There is also a threshold K_I , known as the stress corrosion limit or the fatigue limit, K_{IC} , below which crack growth ceases; however, K_{IC} is usually a practical limit dictated by how low a velocity can be measured, for example, 1×10^{-11} m/s. Information of the type presented in Figure 5 can be used to determine what applied K_I should be used to ensure that no crack propagation occurs, or to predict component lifetime. Materials with low n values are most susceptible to SCG. Values of n range from 15 for soda lime silica glass to 35 for silica glass, and from 90–100 for oxides such as MgO-stabilized ZrO_2 .

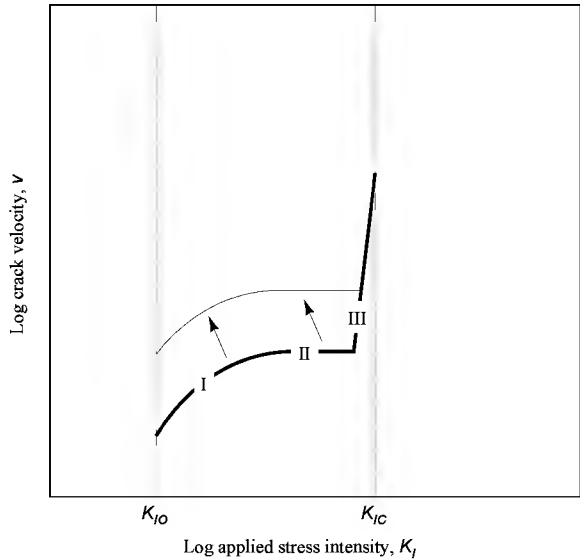


Fig. 7. Crack velocity as a function of the applied stress intensity, K_I . Water and other corrosive species reduce the K_{I0} required to propagate a crack at a given velocity. Increasing concentrations of reactant species shifts curve upward. Regions I, II, and III are discussed in text.

Impact and Erosion. Impact involves the rapid application of a substantial load to a relatively small area. Most of the kinetic energy from the impacting object is transformed into strain energy for crack propagation. Impact can produce immediate failure if there is complete penetration of the impacted body or if the impact induces a macrostress in the piece, causing it to deflect and then crack catastrophically. Failure can also occur if erosion reduces the cross section and load-bearing capacity of the component, causes a loss of dimensional tolerance, or causes the loss of a protective coating. Detailed information on impact and erosion is available (49).

Two types of stress can arise when a ceramic is impacted; a localized stress at or near the impact point, and or a macroscopic stress. In the case of a blunt indenter, a crack called a Hertzian conoid usually forms from excessive tensile stresses around the point of contact. If, after the Hertzian conoid is formed, the impacting object still possesses a significant amount of kinetic energy, further damage may occur in the form of radial cracks and circumferential cracks. Sharp indenter impact can also produce Hertzian cone cracks as shown in Figure 8. If the impact load is relatively large and sustained, a macroscopic stress may be imposed on the target body causing it to bend. This may lead to excessive tensile stresses on the opposite face of the body, crack initiation, and catastrophic failure.

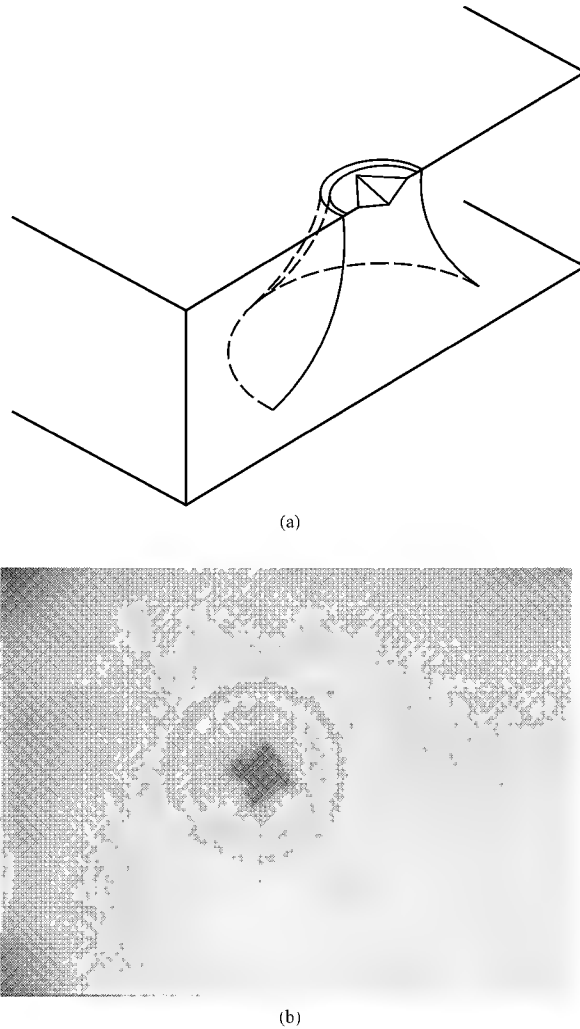


Fig. 8. (a) Schematic of a Vickers indentation-induced Hertzian cone crack. (b) View from the bottom of an aluminosilicate glass block of a Vickers indentation-induced Hertzian cone crack.

External factors affecting a ceramic's response to impact include the velocity, size, and shape of the impacting object, and its angle of incidence. Impacting particles do not have to be hard or tough materials to cause damage and erosion. For instance, water at high velocities, eg, rain on aircraft windshields, can have an extremely erosive effect because of the high localized stresses that it produces. Another mechanism of failure for liquid impact is

the generation of shock waves that interact with pre-existing flaws producing crack growth. Material and microstructural characteristics that influence a ceramic’s impact resistance include density, elastic modulus, crystalline anisotropy, hardness, fracture toughness, strength, grain size, defects such as pores, and the presence of second phases. There are limited data quantifying the relationship between impact strength and microstructural parameters (3).

Impact resistance is determined using flyer plate impact tests, long rod impact tests, Hopkinson bar tests (50), and the liquid jet technique (51). Impact damage resistance is often quantified by measuring the postimpact strength of the ceramic.

Tribological Behavior. Tribological performance of ceramics, which includes friction, adhesion, wear, and lubricated behavior of two solid materials in contact, has been reviewed (52).

Friction and Adhesion. The coefficient of friction μ is the constant of proportionality between the normal force P between two materials in contact and the perpendicular force F required to move one of the materials relative to the other. Macroscopic friction occurs from the contact of asperities on opposing surfaces as they slide past each other. On the atomic level friction occurs from the formation of bonds between adjacent atoms as they slide past one another. Friction coefficients are usually measured using a sliding pin on a disk arrangement. Friction coefficients for ceramic fibers in a matrix have been measured using fiber pushout tests (53). For various material combinations (43):

Materials	μ
clean metals in air	0.8–2
steel on ceramics	0.1–0.5
ceramic on ceramic	0.05–0.5
high temperature lubricants (MoS ₂ , graphite)	0.05–0.2

Factors that affect μ include loading geometry, microstructure, crystal orientation, surface chemistry, environment, temperature, and the presence of lubricants.

Wear. Ceramics generally exhibit excellent wear properties. Wear is determined by a ceramic’s friction and adhesion behavior, and occurs by two mechanisms: adhesive wear and abrasive wear (43). Adhesive wear occurs when interfacial adhesion produces a localized K_I when the body on one side of the interface is moved relative to the other. If the strength of either of the materials is lower than the interfacial shear strength, fracture occurs. Lubricants (see LUBRICANTS AND LUBRICATION) minimize adhesion between adjacent surfaces by providing an interlayer that shears easily. Abrasive wear occurs when one material is softer than the other. Particles originating in the harder material are introduced into the interface between the two materials and plow into and remove material from the softer material (52). Hard particles from extrinsic sources can also cause abrasive wear, and wear may occur in both of the materials depending on the hardness of the particle.

Generally the harder the ceramic, the better its wear resistance; however, other properties such as fracture toughness may play the dominant role. If a ceramic is mated with a metal hardness is the determining factor, but when a ceramic is mated with another ceramic fracture toughness appears to determine the wear rate (54).

Thermal Stresses and Thermal Shock. Thermal stresses arise when a body is heated or cooled and constrained from expanding or contracting. Thermal stresses can lead to fracture and catastrophic failure when the magnitude of the thermal stress exceeds the strength of the ceramic. Factors that contribute to the generation of large thermal stresses and the failure of ceramics under these stresses are low thermal conductivities, which produce large temperature gradients, and the lack of a stress relief mechanism such as plastic deformation. Approaches used to minimize thermal stresses include matching the expansion of ceramics with the expansions of the materials to which they are joined (55), minimizing temperature gradients, minimizing cross-sectional thickness changes to ensure that the body heats or cools uniformly, keeping the body at its operating temperature, and heating and cooling slowly.

Residual thermal stresses can occur in ceramics, especially in glasses, when they are cooled from elevated temperatures, and faster cooling of one region freezes in a structure that subsequently is unable to contract as much as another. This produces a situation at low temperatures wherein the regions that initially cooled more quickly are under compression and the slower cooling regions are under tension. Because tensile stresses are normally undesirable, annealing procedures are used to eliminate the residual stresses. Beneficial residual compressive surface stresses, which effectively strengthen the glass, are produced by a procedure known as thermal tempering.

When heating or cooling is extremely rapid, such as when a body is removed from a furnace and immersed in ice water, large thermal gradients produce very high stresses. Rapid temperature changes, known as thermal shock, can lead to immediate failure of the body, or a degradation in the strength of the body resulting from the generation and propagation of cracks, or the growth of preexisting flaws. Thermal shock resistance (TSR) is the resistance to thermal shock-induced strength changes. TSR is usually quantified in terms of the temperature change, ΔT , below which no strength degradation occurs. An example of a commonly used TSR parameter is

$$\Delta T = \frac{\sigma (1 - \nu)}{\alpha E}$$

(15)

where σ = strength, ν = Poisson’s ratio, α = coefficient of thermal expansion, and E = Young’s modulus. TSR values, calculated using equation 15 and typical values of σ , ν , α , and E are shown in Table 3.

Table 3. Thermal Shock Resistance Parameters

Material	Strength, MPa ^a	Poisson's ratio	Coefficient of thermal expansion, $\times 10^{-6} \text{ }^{\circ}\text{C}^{-1}$	E , GPa ^a	TSR parameter, $^{\circ}\text{C}$
alumina	345	0.22	7.4	380	96
Pyrex	70	0.20	4.6	70	170
silicon carbide	414	0.17	3.8	400	230
Y-TZP ^b	745	0.23	10.5	220	248
silicon nitride	310	0.24	2.4	172	650
LAS ^c	138	0.27	0.3	70	4860

^a To convert MPa to psi, multiply 145,000.
^b Y-TZP = yttria-stabilized tetragonal zirconia polycrystal.
^c LAS = lithium aluminosilicate.

TSR depends on the conditions of thermal shock, the material, and the intended application of the material. TSRs are broadly divided into two groups, those based on conditions under which crack nucleation is favored, and those under which crack propagation is favored. For the former situation high TSRs are found for materials with low E and α , and high σ and thermal conductivity. For conditions favoring crack propagation, high TSRs are found for materials with high E and fracture surface energy, γ , and low σ . A compendium of TSRs is available (56).

TSR is commonly measured by heating ceramics to various temperatures and then quenching them in a liquid medium. The critical temperature

difference ΔT_{crit} , which causes severe damage, is used as a measure of the TSR. A common approach for quantifying the damage from thermal shock is to compare the strength of quenched and unquenched specimens. Another test utilizes thin circular disks heated rapidly with tungsten halogen lamps (57).

Cyclic Fatigue. Cyclic fatigue is the weakening and subsequent failure of a material during cyclic loading, often at stress levels significantly less than that required to cause failure under static loading. Cyclic stresses can be produced by repeated heating and cooling, by vibrations, and in applications in which the component is repeatedly loaded and unloaded. Ceramics were not known to exhibit cyclic fatigue (58) until the late 1980s when it was shown that cyclic fatigue occurs in ceramics under compressive loading (59). In ceramics which show crack interface bridging, cyclic fatigue is largely a result of the loss or destruction of ligamentary bridges when the crack closes. Some of the difficulties in identifying cyclic fatigue mechanisms in ceramics are related to the difficulties in obtaining reliable data using conventional cyclic fatigue testing, in which the failure stress is determined vs the number of cycles to failure. An alternative approach for ceramic cyclic fatigue testing is based on the repeated indentation of a polished surface until chipping occurs (60).

Fracture Analysis

Fracture analysis, also known as fractography, plays an important role in understanding the relationships between structure and mechanical properties, and the conditions that lead to failure (see FRACTURE MECHANICS). Systematic examination and interpretation of fracture markings and the crack path can often be used to reconstruct the sequence of events and stresses that led to failure. Fractography also plays an important role in the intelligent use of ceramics because it helps the user differentiate whether failure occurred because the material was weakened by the introduction of processing and handling flaws, or because the applied stress exceeded the design stress.

Well-established fractographic techniques are available for determining crack propagation direction, failure origin location, estimating the failure stress, identifying what types of flaws are present, and for identifying local events that initiated failure, eg, impact or thermal shock (42,61,62). A significant amount of information about crack growth and failure can be determined using the fracture surface markings and the crack path. Some of the most useful fracture markings include the fracture mirror, mist, and hackle, so called because these three terms aptly describe the fracture surface appearance, especially for glasses; crack branching patterns; Wallner lines; and arrest lines. Some of these features can be seen on the fracture surface shown in Figure 9. Fracture surface markings are influenced by, and therefore can provide information about the stress magnitude, crack velocity, interactions of the crack with microstructural inhomogeneities and stress pulses, flaw size and shape, and the test environment. The crack path provides information about the stress state at different positions in the body. The crack pattern can be a good indication of the conditions the gave rise to a certain stress state, such as thermal shock, impact, and twisting.

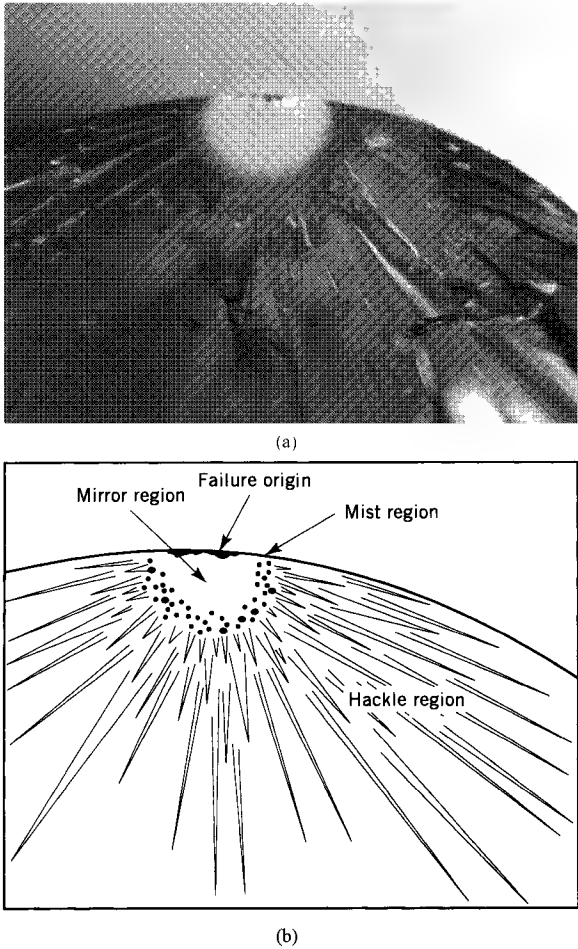


Fig. 9. (a) Optical micrograph of the fracture surface of a glass rod at 38 X. (b) Characteristic fracture markings such as mirror, mist, and hackle and the failure origin are indicated on the fracture surface schematic.

Fracture markings can be used to locate the failure origin, which is the discontinuity or flaw that caused the applied stress to be amplified locally. Once the failure origin has been located, the failure stress can be estimated using the flaw size and equation 6, or the distances to the boundaries of the mirror, mist, and hackle (whichever is most evident) and the following relation (63)

$$\sigma_{fracture} \sqrt{r_i} = A_i \tag{16}$$

where r = radius; A = constant (values for various ceramics can be found in the literature (64) and; i = 1, 2, or 3 (refers to the mirror, mist, and hackle boundary). If the ceramic body is small and the failure stress is extremely low, the mirror may extend over the entire fracture surface, and mist and hackle are absent.

Most fractography can be conducted with simple instruments such as a pocket magnifying eyepiece or an optical microscope. As with any detective work, it is important to maintain careful records and to pay close attention to details in the reconstructions of the conditions under which fabrication and failure occurred. Seemingly unimportant details of fabrication, service, and or the conditions under which failure occurred can frequently be the key to determining the cause of failure.

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GLASS STRUCTURE AND PROPERTIES

Inorganic glasses are important ceramic materials and glasses share many of the desirable properties of crystalline ceramics even though they lack long-range order (see GLASS; GLASS, CERAMICS). The structure of glasses is not completely random, however. Glasses do have short-range order in the arrangement of anions around cations.

Glasses, less thermodynamically stable than crystals, must be "captured" in a metastable state, and this is typically accomplished by rapid cooling of a liquid. Whereas virtually any inorganic material can form a glass if it can be cooled at a sufficiently rapid rate, glasses requiring extremely fast cooling rates such as those attained from splat quenching or twin-roller techniques are not discussed herein.

Types of Glasses

The simplest inorganic glasses are composed of only one element: B, C, P, As, S, or Se. Glassy selenium in thin-film form has been used extensively in the photocopying industry. Inorganic glasses containing more than one element can be broadly categorized according to the type of anion. There are two main categories: chalcogenide glasses and halide glasses. Chalcogenide glasses contain anions from Group 16 (VI A) of the Periodic Table O, S, Se, Te; halide glasses contain anions from Group 17 (VII A), F, Cl, Br, I. Although oxide glasses are, strictly speaking, a subset of the chalcogenide glasses, the family of oxide glasses is so large and so important that it is usually considered separately from the other chalcogenides.

Oxide Glasses. The oxides that form glass without the addition of any other agents are known as primary glass forming oxides. These are P₂O₅, As₂O₅, SiO₂, GeO₂, and B₂O₃. Vitreous arsenious oxide, As₂O₃, is obtained by condensing the vapor onto a cold surface. It is possible to form small amounts of antimony trioxide glass by sealing Sb₂O₃ into a silica ampul which is heated to 800°C for 30 minutes and then quenched by being held in contact with a cold metal plate. Sulfur trioxide also forms a glass when cooled rapidly to a temperature below its melting point of 16.8°C. The most important, by far, of all the glass forming oxides is silicon dioxide, SiO₂. The oxides V₂O₅ and TeO₂ form glasses with very small (<5 mol %) amounts of additives. In general, an oxide compound that is capable of contributing over 50 atom % of the cations in a glass is known as a conditional glass former. These include MoO₃, WO₃, TiO₂, Fe₂O₃, Al₂O₃, Ga₂O₃, Bi₂O₃, BeO, and PbO. The compounds Nb₂O₅ and Ta₂O₅ can form glasses in proportions up to 42.5 mol %.

Nonoxide Chalcogenide Glasses. Primary glass forming sulfides include As₂S₃, SiS₂, GeS₂, B₂S₃, Al₂S₃, Ge₂S₃, As₂S₃, and Sb₂S₃. Arsenic(III) sulfide is the most widely known and used sulfide glass, but its manufacture is problematic because of the toxicity and volatility of arsenic. The compounds P₂S₅, Ga₂S₃, and In₂S₃ are conditional glass forming sulfides. Some primary glass forming selenides are SiSe₂, GeSe₂, Ge₂Se₃, As₂Se₃, Sb₂Se₃, and TlSe. Examples of primary glass forming tellurides are GeTe₂, Si₂Te₃, GaTe, GeTe, and SnTe. The compound As₂Te₃ is glassforming (1), but the glass is difficult to obtain. Some compounds, such as Ge₂S₃, Ge₂Se₃, and GeTe₂, do not exist in crystalline form. In general, nonoxide chalcogenide glasses can exist over wide ranges of the component elements. For example, the S/Ge ratio in binary Ge–S glasses can range from 1.3 to 1.5 and from 2 to 9. Chalcogenide glasses containing various ratios of three elements include Ge–As–S, Ge–As–Se, Ge–As–Te, Ge–Sb–Se, As–Sb–Se, As–S–Se, As–S–Te, As–Se–Te, S–Se–Te, etc. Mixed chalcohalide glasses such as Se–Te–X (X = Cl, Br, I) have also been developed.

Halide Glasses. Fluoride glasses are the most important of the halide glasses. The only primary fluoride glass former is beryllium fluoride, BeF₂ (see BERYLLIUM COMPOUNDS). Conditional fluoride glass formers are ZrF₄, HfF₄, ThF₄, UF₄, ScF₃, YF₃, CrF₃, FeF₃, AlF₃, GaF₃, InF₃, ZnF₂, CdF₂, and PbF₂. The only primary chloride glass former is zinc chloride, ZnCl₂. Conditional chloride glass formers include ThCl₄, BiCl₃, CdCl₂, SnCl₂, PbCl₂, CuCl, AgCl, and TiCl. The only primary bromide glass former is zinc bromide, ZnBr₂, which is more difficult to prepare than is ZnCl₂. Conditional bromide glass formers include PbBr₂, CuBr, and AgBr. Conditional iodide glass formers include ZnI₂, CdI₂, PbI₂, CuI, and AgI. There are many mixed-halide glasses (2,3).

Oxyhalide Glasses. Many glasses contain both oxide and halide anions. The introduction of halides into an oxide glass typically serves to reduce the glass-transition temperature, *T_g*, and to increase the coefficient of thermal expansion. Oxyfluorophosphates have been investigated as laser host materials. The Sn–P–O–F system yields glasses having very low glass-transition temperatures and moderate durability in water. Relatively large amounts of halides can be incorporated into glasses based on tellurium(IV) oxide or antimony(III) oxide.

Oxynitride Glasses. Small concentrations of nitride ions, sometimes added as Si₃N₄ or AlN, increase the viscosity of oxide melts, the refractive index, *T_g*, and hardness of oxide glasses. Apparently the nitride anions are three-coordinate and cause more cross-linking and denser packing in the glass. The incorporation of large amounts of nitrogen also increases the tendency for the glasses to crystallize.

The first oxynitride glasses were aluminosilicates; these Si–Al–O–N glasses became known as sialons. Much greater concentrations of nitrogen (up to 15 atomic %) can be accommodated in magnesium, calcium, yttrium, or rare-earth sialons. The glasses are bluish gray, and the color intensifies with nitride concentration. The crystallization products are high melting oxynitride compounds, so it is possible that the sialon glasses could give rise to glass-ceramics with useful high temperature properties.

Other glasses, such as phosphates and borates, have also been nitrified. The nitridation improves the aqueous durability of the parent glass. In low melting nonsilicate glasses, the nitride ions are typically introduced into the glass by melting in an ammonia atmosphere or by bubbling ammonia through the melt.

Oxycarbide Glasses. Oxycarbide silicate glasses are made by adding SiC to the melt. The *T_g* and hardness of the glasses are increased to a greater extent than by nitride additions, because the carbide anion is four-coordinate and results in a greater degree of cross-linking. The density, elastic modulus, and fracture toughness increase with increasing carbon content.

Glasses Containing Polyatomic Anions. Carbonate, nitrate, nitrite, sulfate, dichromate(VI), and selenate(IV) glasses are interesting in that they contain discrete polyatomic anions rather than extended oxide networks (4). Structural interpretations of glass formation in these systems usually are based on the idea that unbalanced cation force fields prevent efficient packing of polyatomic anions, which are typically triangular, pyramidal, or tetrahedral. There are many cases of mixed-anion glasses containing combinations of halides and polyatomic anions (4). Most of these glasses are quite soluble in water.

Carbonate Glasses. Carbonate glasses must be melted under moderate pressures to prevent the escape of carbon dioxide gas. The simplest carbonate glass forming system is K₂CO₃–MgCO₃.

Nitrate and Nitrite Glasses. The best nitrate glasses result when the difference between the field strengths (*Z/r*²) of the cations is 0.7 or more (4). Here, Z is the charge on the cation, and *r* is the cation radius in nm × 10^{–1}. Cations having high field strengths tend to cause perturbations of the symmetry of the nitrate ions. The most studied nitrate composition is 40Ca(NO₃)₂·60KNO₃. Nitrate glasses containing large amounts of thiocyanate (SCN[–]) also exist. Nitrite glasses such as those in the Ca(NO₂)₂–KNO₂ system have been prepared, but decomposition of nitrite melts is a problem.

Sulfate Glasses. The sulfate ion is tetrahedral (quasispherical), so the formation of sulfate glasses is more difficult than the formation of nitrate glasses (4). The presence of cations of different valences appears to be necessary for sulfate glasses. An example is the ZnSO₄–K₂SO₄ system. Glass

formation is enhanced upon the addition of chlorides.

Dichromate(VI) Glasses. Alkali dichromate(VI) glasses exist in systems such as $\text{Li}_2\text{Cr}_2\text{O}_7\text{--Na}_2\text{Cr}_2\text{O}_7$. The glass-transition temperatures of the dichromates are very low, about 0°C. The addition of chlorides or nitrates aids in glass formation.

Selenate(IV) Glasses. Selenate(IV) glasses, like carbonate glasses, are very volatile. They are best prepared under pressure. Sublimation from glasses in the $\text{K}_2\text{O--SeO}_2$ system, however, has been reported to be negligible. The selenate(IV) glasses have low glass-transition temperatures and are very hygroscopic.

Glass Structure

Several criteria for predicting which compounds form glasses have been proposed. The best known guidelines are those originally presented for oxide glasses and known as Zachariasen Rules (5). They can be summarized as: (1) an oxygen or anion must not be linked to more than two cations; (2) the oxygen or anion coordination number of the cations must be small; and (3) the cation–anion polyhedra must share corners rather than edges or faces. These rules are satisfied by glasses such as vitreous B_2O_3 , which contains triangularly coordinated boron atoms, and by vitreous SiO_2 and vitreous BeF_2 , which both contain tetrahedrally coordinated cations. Many fluoride glasses, such as those based on zirconium(IV) fluoride, ZrF_4 , contain cations having high coordination numbers of 6, 7, or 8 (see FLUORINE COMPOUNDS, INORGANIC) and thus violate Rule 2. However, the fluoride ions are predominantly two-coordinate, as required by Rule 1. The importance of Rule 1 in glass formation is probably because a distribution of M--A--M angles, where M is a cation and A is an anion, is necessary to avoid imposing too much order in the system. If most of the anions were, for example, three-coordinate, there would be little structural freedom in the network, and the substance would crystallize. Both crystalline and vitreous SiO_2 are shown in Figure 1.

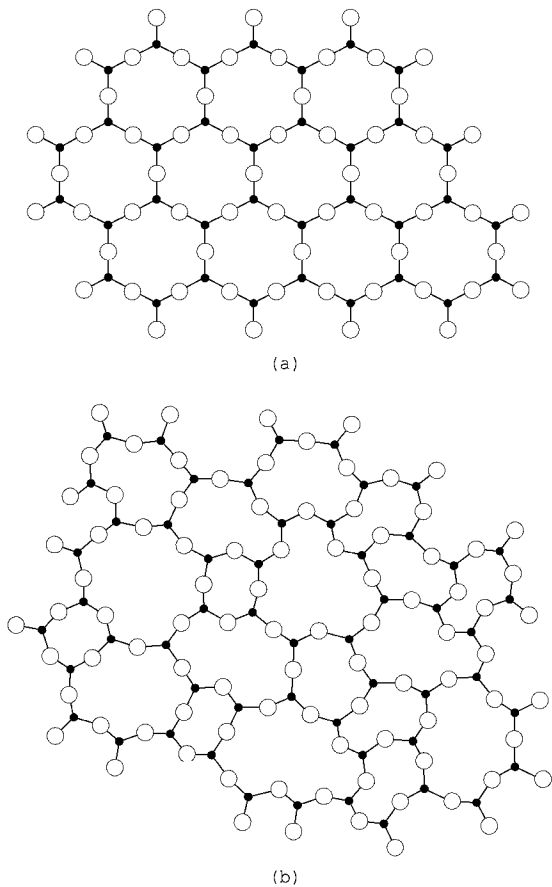


Fig. 1. Schematic two-dimensional representation of SiO_2 structures where ● represents Si atoms and ○, oxygen, (a) crystalline material; (b), glass (5).

The radius ratio rule (6) can be used with Zachariasen Rule 1 to predict which compounds tend to form glass. For oxides with the formula MO_2 , charge balancing requires that the cations must be four-coordinate if the oxygens are to be two-coordinate. For tetrahedral coordination of a cation by oxygen, the ratio of the cation radius to the oxygen radius must be <0.414 (6). Oxides satisfying this requirement are SiO_2 and GeO_2 , which are glass forming. The radius ratio of TiO_2 is too large, but glasses containing substantial amounts of TiO_2 can be made if other agents are added. Whereas the radius ratio of Te^{4+} is much too large, glasses containing as much as 98 mol % TeO_2 have been reported, presumably because the Te^{4+} lone pair of electrons occupies a large amount of space allowing the tellurium cation to be four-coordinate.

For halides the cation should have a charge of 2+ rather than 4+ for tetrahedral coordination. The only fluoride compound capable of containing two-coordinate F and four-coordinate cations is BeF_2 . For ZrF_4 , the radius ratio rule predicts that Zr^{4+} is eight-coordinate if all fluorine atoms are two-coordinate.

In addition to the Zachariasen and radius ratio rules, for oxides the electronegativity of the predominant cation should be between 1.7 and 2.1 (7). If the cation electronegativity is too high, the compound tends to form molecules or discrete polyatomic ions rather than a connected network. For example, CrO_3 satisfies the radius ratio rule, but the highly electronegative Cr^{6+} ions promote the formation of discrete dichromate(VI) ions, $\text{Cr}_2\text{O}_7^{2-}$; in the presence of other oxides.

Modifiers in glass are compounds that tend to donate anions to the network, whereas the cations occupy "holes" in the disordered structure. These conditions cause the formation of nonbridging anions, or anions that are connected to only one network-forming cation, as shown in Figure 2. Modifier compounds usually contain cations with low charge-to-radius ratios (Z/r), such as alkali or alkaline-earth ions.

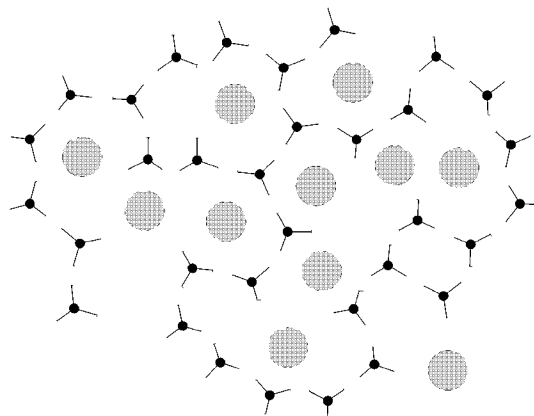


Fig. 2. Schematic two-dimensional representation of the structure of sodium silicate glass where ● represents Si; ○, oxygen; and ● sodium (5).

Optical Properties

Probably the most striking and useful characteristic of common silicate glass is its transparency to visible light. This transparency results from the absence of grain boundaries and delocalized electrons, which tend to scatter and absorb light.

Transmission of Light. In the absence of an electromagnetic field, the electrons and atoms of a material oscillate at their natural, or resonance, frequencies. When the frequency of an incident electromagnetic field matches the resonance frequency of any of the components, some of the light is absorbed. This frequency is determined by the constituents and the chemical bonds. Absorption in the ultraviolet (uv) is primarily from electronic transitions associated with the oxygen atoms, particularly nonbridging oxygens. The addition of alkali or alkaline-earth oxides to a glass forming oxide shifts the uv absorption edge to lower energies (longer wavelengths). Conversely, the range of uv transmission is enhanced when the cations in the glass have a high charge-to-radius ratio, indicating a stronger cation–oxygen bond.

When equimolar quantities of a given modifier oxide are added to SiO_2 and B_2O_3 , the uv cutoff of the silicate glass is at a lower energy than that of the borate; the value of Z/r for Si^{4+} is 10, and the Z/r of B^{3+} is 20. The addition of nitride ions to oxide glasses shifts the uv edge to longer wavelengths (lower energies), probably because of the greater polarizability of the trivalent nitrogen.

In the visible region, absorption by additives such as transition-metal or lanthanide ions is usually more important than contributions from the glass formers themselves. The solarization, ie, coloration of glass by uv radiation from sunlight, usually results from oxidation of transition-metal ions in the glass. However, gamma rays or x-rays can induce coloration even in undoped glass through the formation of separated electron-hole pairs. Binary phosphovanadate glasses are opaque in the visible region because of the movement (delocalization) of electrons between V^{5+} and V^{4+} sites. Chalcogenide glasses such as As_2S_3 are colored or even opaque, because of the small difference in energy between the conduction and valence bands.

Glasses having some absorption in the visible are used in products such as sunglasses. The visible transmission of photochromic glasses decreases with increasing frequency of light, and the effect is reversible. These glasses contain small (~ 10 nm in diameter) droplets of silver chloride, AgCl , or other silver halides doped with copper(I) ions (8). In the presence of uv radiation, the reaction $\text{Ag(I)} + \text{Cu(I)} \rightarrow \text{Ag} + \text{Cu(II)}$ occurs, leading to the formation of small particles of metallic silver which cause the glass to darken.

Infrared (ir) transmission depends on the vibrational characteristics of the atoms rather than the electrons (see INFRARED AND RAMAN SPECTROSCOPY). For a diatomic harmonic oscillator, the vibrational frequency is described by

$$\nu = \frac{1}{2\pi c} \left(\frac{k}{\mu} \right)^{1/2}$$

where ν is the frequency, c is the speed of light, k is the force constant of the bond, and μ is the reduced mass of the atoms. Thus the ir cutoff in a glass would be extended to lower energies as the atomic masses increase and as the bond strengths decrease and indeed germanate glasses transmit further into the ir than silicate glasses because germanium atoms are larger and heavier. Also, halide glasses have better ir transmission than oxide glasses; the -1 charge on the halide ions leads to weaker cation–anion bonds. Chalcogenide glasses combine the desirable features of heavy atoms and low valent ions. For example, the well-known infrared optical component material As_2S_3 transmits at longer wavelengths than GeO_2 does because As is heavier than Ge, S is heavier than O, and the arsenic ion has a charge of $3+$ as opposed to the charge of $4+$ on germanium.

Refractive Index. The refractive index n of a glass is defined as the ratio of the speed of light in vacuum to the speed of light in the glass, $n = c/v$. The value of n is always greater than 1, because light travels more slowly in dense media. The refractive index is governed almost exclusively by the nature of the electron-oscillators, with essentially no contribution from atomic vibrations. At visible frequencies, the electrons of an optically transparent glass can follow or move in phase with the applied field, but because of the small vibrational amplitudes of these induced oscillations, the light is reradiated rather than absorbed.

The loosely bound valence electrons make the greatest contribution to n , so large, many-electron atoms, eg, Pb(II) or Bi(III) , are added to glass to increase the refractive index. For Pb(II) or Bi(III) additions, there is a lone pair of nonbonding electrons that are exceptionally polarizable and contribute to n even more effectively than the other valence electrons. In general, the refractive index of a glass also increases on addition of alkali oxides, because of the formation of polarizable nonbridging oxygens. The partial replacement of oxide ions by fluoride ions decreases n because the small, electronegative fluoride ions bind electrons tightly. The substitution of nitride ions for oxide ions results in an increased refractive index because of the greater negative charge and lower electronegativity of nitrogen. Addition of PbO to silicate glass creates lead crystal.

Dispersion. A glass prism separates white light into its component colors by virtue of the frequency dependence of n . The higher the frequency, the higher the refractive index for a given substance, ie, blue light is slowed to a greater extent than red light and deviated through a larger angle by a prism. It is this dependence of the refractive index on the frequency (color) of light that is known as dispersion. The measure of dispersion is the Abbñ number, ν_d , which is equal to $(n_d - 1) / (n_F - n_C)$ where n_d , n_F , and n_C are the indexes of refraction at the sodium d -line (587.6 nm), a wavelength in the blue (486.1 nm), and a wavelength in the red (656.3 nm), respectively. The greater the dispersion, the smaller the Abbñ number.

A low dispersion is desirable in optical glasses used for lenses in cameras, telescopes, etc, because dispersion causes chromatic aberration, a condition which reduces the sharpness of an image. However, it is possible to correct for chromatic aberration by using a combination of glasses having different Abbñ numbers (9).

The farther into the uv and the narrower the distribution of the resonant electron frequencies, the smaller the effect of dispersion in the visible region. The Pb(II) ion exhibits absorption in the near-uv, and addition of Pb(II) to a glass increases both n and dispersion. However, the use of Ba(II) and La(III) increases n without increasing dispersion. Fluorophosphates, having absorption bands located well into the uv, are examples of glasses with high Abbñ numbers and low refractive indexes.

Fluorescence and Glass Lasers. Some ions absorb light of a certain frequency emitting light of lower frequency. This is known as fluorescence. Examples of ions that fluoresce in glass are Mn(IV) , Pb(II) , and the lanthanide ions.

The existence of glass lasers (qv) was first reported in 1961 (10). Optically pumped laser action has since been observed for several lanthanide ions in a variety of glass systems (11). Large, high power neodymium glass lasers have been used for inertial confinement fusion experiments (11). The best glass laser systems have the following qualities: the absorption spectrum of the lasing ion matches the spectrum of the pump radiation; the absorbed radiation efficiently produces excited-state ions; the excited state has a long lifetime; the probability of radiative decay is high; and the linewidth of the emitted radiation (fluorescence) is narrow. The linewidth of the fluorescence band of the lanthanide ion is affected by the glass matrix. In general, the smaller the field strength of the anions, the less the perturbation of the coordination shell of the fluorescing ion and the narrower the linewidth, ie, fluoride and chloride glasses promote narrower linewidths than those seen in oxide glasses. The stimulated-emission cross sections (efficiencies) of rare-earth sulfide glasses based on Ga₂S₃ are reported to be higher than those of oxide, oxyhalide, and halide glasses (12).

Electrical Properties

There are many applications in which glass is used as an electrical insulator. One example is glass-to-metal seals. Moreover, other glasses are useful as a result of ionic or electronic conductivity.

Ionic Conductivity. Ionic conductivity in oxide glasses is almost always because of the movement of monovalent cations, eg, in an alkali silicate glass, the small, univalent alkali ions are much more mobile than the Si⁴⁺ or O²⁻ ions. In glasses containing appreciable amounts of hydroxide groups, charge can be carried by H⁺ ions. The ions move through the glass network when subjected to an applied field, so the ionic conductivity of a glass depends on the distribution of ring sizes (or doorways) in the glass as well as on the size, charge, and polarizability (deformability) of the charge carriers. For a given glass network and a given charge on the mobile ions, smaller ions fit through the doorways more easily, but their higher field strength causes greater interactions with the network and tend to increase the activation energy for movement. For a given ion, sulfide glasses have higher ionic conductivities than oxide glasses, because the larger, more polarizable sulfide ions deform more easily than do oxide ions.

The electrical conductivities of many glasses containing monovalent ions are so high that such glasses are being considered for all-solid-state batteries (qv). An example of a highly conductive sulfide-based glass is the Li₂S–P₂S₅–LiI system. The glass family exhibiting the highest ionic conductivities is based on AgI–AgMO_x, where M = Cr, Mo, B, P, As, or Se. The conductivities of these glasses at 25°C can be as high as that of a 0.1 M aqueous solution of KCl. Batteries based on these systems have been made, but are not of commercial interest because of low energy density.

Semiconductivity. Amorphous selenium and other chalcogenide glasses form the basis for the multibillion dollar electrostatic copying industry (see ELECTROPHOTOGRAPHY). Although amorphous substances possess only short-range and a certain degree of intermediate-range order, they can exhibit extended electronic states similar to those found in crystals. Glassy semiconductors (qv) also possess localized electronic states. There is no energy gap between the localized and extended states, but at a certain boundary energy E_c there is an abrupt change in mobility between the states, leading to a mobility gap. This means that the localized states effectively act as traps for charge carriers. Conduction in chalcogenide glasses can occur by the activation of carriers across the mobility gap into the extended states, or by tunneling between the localized states. Conduction is favored if the atoms are close together and if the spatial extent of the overlapping orbitals is relatively large. For example, the conduction band is more likely to consist of *p*-orbitals than *s*-orbitals.

It has been known since the 1960s that certain chalcogenide glasses can be switched between low and high conductivity states using an applied voltage. There are two types of switching: threshold and memory. In the case of threshold switches, a small current is required to maintain the on (high conductivity) state. In contrast, memory switches remain on indefinitely in the absence of a current and require a short, high current pulse to return to the off state. A typical glass for a memory switch contains Ge, Te, and either As, S, or Sb. The on state in threshold switching is thought to arise from the saturation of charged defect centers. This same state in memory switching has been attributed to the formation of a conductive crystalline filament. The filament is remelted to the glassy state with the applied pulse.

Semiconductivity in oxide glasses involves polarons. An electron in a localized state distorts its surroundings to some extent, and this combination of the electron plus its distortion is called a polaron. As the electron moves, the distortion moves with it through the lattice. In oxide glasses the polarons are very localized, because of substantial electrostatic interactions between the electrons and the lattice. Conduction is assisted by electron-phonon coupling, ie, the lattice vibrations help transfer the charge carriers from one site to another. The polarons are said to "hop" between sites.

Cations capable of multiple valences facilitate small-polaron conductivity. Vanadium and tungsten ions readily assume multiple valences, and vanadium oxide and tungsten oxide glasses exhibit some of the highest electrical conductivities of any oxide glass. Phosphate and tellurate(IV) glasses containing substantial amounts of multiple-valent transition-metal ions such as iron or copper are also semiconducting. The conductivity is enhanced if the transition-metal ions are close together, the ionic charges are small, and the spatial extent of the *d*-orbitals is large.

Dielectric Constant. Capacitance, *C*, refers to the ability of two conductors to store charge, *Q*, in the presence of a potential difference, *V*; *C* = *Q* / *V*. In a vacuum, the charge density on the surfaces of the conductors is affected by the permittivity of free space, ε₀. When a dielectric material is placed between the conductors, the capacitance increases because of the higher permittivity, ε, of the material. The ratio of ε and ε₀ gives the dielectric constant, κ, of the material, κ = ε / ε₀. The dielectric constant of silica glass is 3.8.

The dielectric constant is a measure of the ease with which charged species in a material can be displaced to form dipoles. There are four primary mechanisms of polarization in glasses (13): electronic, atomic, orientational, and interfacial polarization. Electronic polarization arises from the displacement of electron clouds and is important at optical (ultraviolet) frequencies. At optical frequencies, the dielectric constant of a glass is related to the refractive index: κ = *n*². Atomic polarization occurs at infrared frequencies and involves the displacement of positive and negative ions.

At lower frequencies, orientational polarization may occur if the glass contains permanent ionic or molecular dipoles, such as H₂O or an Si–OH group, that can rotate or oscillate in the presence of an applied electric field. Another source of orientational polarization at even lower frequencies is the oscillatory movement of mobile ions such as Na⁺. The higher the amount of alkali oxide in the glass, the higher the dielectric constant. When the movement of mobile charge carriers is obstructed by a barrier, the accumulation of carriers at the interface leads to interfacial polarization. Interfacial polarization can occur in phase-separated glasses if the phases have different dielectric constants.

Because κ is related to the polarizability per unit volume, denser glasses generally have higher dielectric constants. The dielectric constant also increases with increasing temperature, because ionic motion becomes faster. Similarly, κ is higher at lower frequencies, because the ions can follow the oscillations more readily.

In a sinusoidally varying field, there are dielectric losses arising from the long-range migration of charges and from overcoming the inertial resistance to the rotation or oscillation of dipoles. Energy losses are minimized when the dielectric constant is small.

Thermal Properties

Glass-Transition Temperature. When a typical liquid is cooled, its volume decreases slowly until the melting point, *T_m*, where the volume decreases abruptly as the liquid is transformed into a crystalline solid. This phenomenon is illustrated by the line ABCD in Figure 3. If a glass forming liquid is cooled below *T_m* (B in Fig. 3) without the occurrence of crystallization, it is considered to be a supercooled liquid until the glass-transition temperature, *T_g*, is reached. At temperatures below *T_g* the material is a solid.

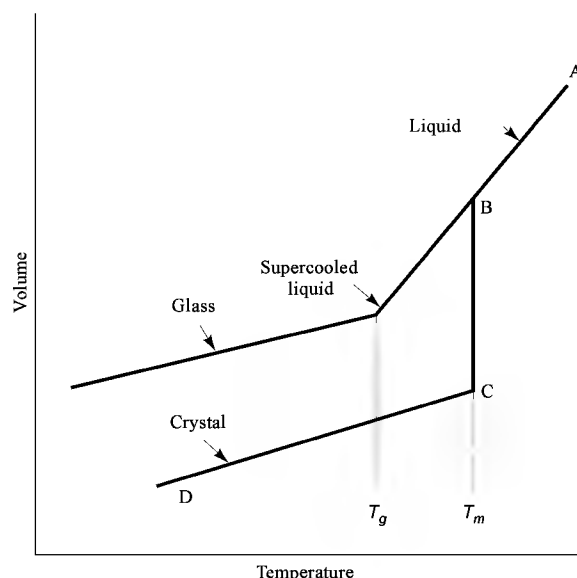


Fig. 3. Volume changes in the glassy, liquid, and solid states. Terms defined in the text.

Courtesy of Chapman & Hall.

Unlike the abrupt melting of a crystalline solid, the glass transition is characterized by a continuous change in properties over a small temperature interval. When a solid glass is heated from below its glass-transition temperature, the volume and specific heat increase slowly. As the glass-transition temperature is reached, the rates of change of these quantities become larger, indicating that bonds are being broken and that some parts of the glass have become more mobile; ie, above T_g the behavior of the glass becomes more like that of a liquid, in that there are now opportunities for long-range molecular diffusion. Viewed in terms of percolation theory, the glass-transition temperature represents the point at which, upon heating, a single liquidlike cluster that spans the entire sample is created.

Glass-transition temperatures are usually proportional to melting temperatures and are dependent on similar factors. For instance, stronger bonds typically lead to higher values of T_g . Although SiO_2 and GeO_2 glasses have virtually the same structure, the T_g of SiO_2 is 1157°C as opposed to only 547°C for GeO_2 because the Ge–O bonds are longer and weaker than the Si–O bonds. The T_g is expected to decrease as modifying agents such as Na_2O are added because of the formation of nonbridging oxygen atoms. The longer-range structural features of a glass also affect transition temperatures.

Working, Softening, Annealing, and Strain Points. Although the glass-transition temperature is important in the scientific study of glass formation, other temperatures are more useful from a technological point of view. For example, the working point refers to the temperature at which the glass can be formed into some desired shape. The American Society for Testing and Materials (ASTM) defines such phrases in terms of viscosity. The working point of a glass corresponds to a viscosity of 10^6 mPas (cP). At the softening point (viscosity of 10^6 Pas), a glass suspended at two points can begin to sag in a few minutes. The term annealing point is essentially the same as T_g . If annealing is carried out at the strain point, a temperature below T_g at which the viscosity is $10^{13.5}$ Pas, the reduction of stresses to acceptable levels takes about four hours.

Thermal Expansion. In general, solids expand when they are heated either through bond length expansion, bond angle changes, or expansion regulated by weak forces such as van der Waals bonding. In a covalently bonded glass such as vitreous SiO_2 , which contains strong Si–O bonds and tetrahedrally coordinated Si atoms, the contribution to the coefficient of thermal expansion (CTE) from bond length expansion is relatively low. The Si–O–Si bond angle changes are important. High silica glasses such as Pyrex have low CTEs and are used in applications requiring good resistance to thermal shock. In fact, certain ultralow expansion SiO_2 – TiO_2 glasses have CTEs of practically zero. Some applications, such as glass-to-metal seals, depend on glasses having high CTEs. Lead-containing glasses are appropriate for such purposes, because the Pb–O bonds are relatively weak and the Pb(II) coordination sphere is quite asymmetric, as a result of the presence of a lone pair of nonbonding electrons.

Thermal Conductivity. Like thermal expansion, thermal conductivity depends on bond anharmonicity, but thermal conductivity is reduced rather than enhanced by the anharmonic contributions. The thermal conductivity also appears to be greatly dependent on long-range order, meaning that an amorphous material has the same effect on phonons as would a greatly anharmonic crystal. The mean free path of a phonon in a glass is on the order of a few interatomic spacings, so phonons are damped out over very short distances, ie, glasses are good thermal insulators, making them ideal materials for windows in buildings. The thermal conductivity of a glass increases markedly as it is crystallized to form a glass–ceramic. The thermal conductivity of an aerogel is exceptionally low.

Processing

Melt Processing. In melt processing, the starting materials, such as powdered oxides or glass pieces from previous melts, are placed into a crucible and heated until the entire mixture is molten. After the melt becomes homogeneous, the liquid is poured into a mold and the resulting glass is then annealed at or slightly below its glass-transition temperature. This approach, although simple and convenient, has some drawbacks: (1) the amount of energy required to prepare the glass is fairly large, especially if the glass is high melting; (2) the temperatures involved can cause unwanted chemical reactions such as oxidation–reduction processes within the melt or with the atmosphere, as well as corrosion of the crucible; (3) some compounds become excessively volatile at elevated temperatures and are lost from the melt; and (4) glasses having relatively large coefficients of thermal expansion may crack before or during the annealing step.

Some ultrafast quenching procedures used for molten materials include: (1) melt spinning, in which a molten metal is ejected onto a rapidly spinning cylinder to form a thin ribbon; (2) splat quenching, in which the melt is smashed onto an anvil by a compressed-air-driven hammer; (3) twin-roller quenching, in which the melt is forced between two cylinders rotating in opposite directions at the same speed; (4) laser glazing, in which a short, intense laser pulse is focused onto a very small volume of a sample; and (5) laser-spin melting, in which a rapidly rotating rod of the starting material is introduced into a high power laser beam, eg, a CO_2 laser, causing molten droplets to spin off and form into small glass spheres (14).

Sol-Gel Processing. In the sol–gel method, a room temperature solution of one or more soluble glass precursor compounds, typically metal alkoxides (see ALKOXIDES, METAL), undergoes hydrolysis to form a metal hydroxide or metal oxide (see SOL–GEL TECHNOLOGY) (15). The by-product is an alcohol that is removed by subsequent heating. The hydrolysis reaction sometimes requires an acid or base catalyst. If unstable metal hydroxides are formed, they can condense together to form M–O–M linkages. Eventually, the colloidal suspension (sol) polymerizes to such an extent that it becomes insoluble and forms a gel. The gel must be dried and then heated to a temperature slightly above the T_g of the corresponding melt-prepared glass to effect densification. If the gel is dried by evaporation under normal conditions, the resulting product is called a xerogel. If instead the gel is dried under supercritical conditions in an autoclave by a fluid such as CO_2 , the resulting product is an aerogel. The preparation of aerogels results in considerably less shrinkage because the surface tension of a supercritical fluid is zero, so it is easier to prepare crack-free samples from aerogels.

Glasses formed by the sol–gel method are very homogeneous and can be made very pure. In general, there is little or no difference between the physical properties of sol–gel and melt-formed glasses of identical composition, but some researchers have reported structural differences. One drawback

to the sol–gel method is the possibility of a higher content of hydroxyl groups or the presence of organic residue in the resulting glass. Another is the expense of the raw materials. An advantage of sol–gel processing is the ability to form thin films (qv) and coatings (qv), in addition to bulk glass articles.

Vapor-Phase Processing. Optical fiber preforms are prepared by vapor-phase techniques because of the superior clarity of the products. This technology also allows the control of refractive index profiles by doping. All vapor-phase techniques use a vapor stream of volatile halides such as SiCl₄, GeCl₄, BCl₃, or POCl₃, and gases such as Cl₂ or O₂. The reactants are oxidized and deposited onto a substrate to produce a solid glass preform which is then drawn into a fiber. The variations of the technique differ in the way the reactants are oxidized (16).

In flame hydrolysis, the halide vapors are converted to oxides in a methane–oxygen flame. The finely divided oxide soot is deposited onto a substrate such as a rotating alumina rod. The refractive index of the glass layers is changed during the deposition by controlling the relative amounts of the halides added to the flame. When the deposition is complete, the rod, which has a higher coefficient of thermal expansion than the deposited material, is removed. The porous glass preform is baked to remove impurities such as water, then sintered into bulk glass.

In the modified chemical vapor deposition (MCVD) technique, the reactants are deposited on the inside of a rotating silica tube. The hollow tube is heated from the outside by a moving oxyhydrogen torch. The oxide soot condenses onto the tube walls ahead of the burner, and the soot is then sintered into a glassy layer as the burner passes over it. When deposition is complete, the tube and its contents are collapsed to form a solid preform rod.

In plasma chemical vapor deposition (PCVD), the starting materials are typically SiCl₄, O₂, C₂F₄, and GeCl₄ (see PLASMA TECHNOLOGY). Plasma chemical vapor deposition is similar to MCVD in that the reactants are carried into a hollow silica tube, but PCVD uses a moving microwave cavity rather than a torch. The plasma formed inside the microwave cavity results in the deposition of a compact glass layer along the inner wall of the tube. The temperatures involved in PCVD are lower than those in MCVD, and no oxide soots are formed. Also, the PCVD method is not affected by the heat capacities or thermal conductivities of the deposits.

Thin-Film Techniques. Many integrated optical and electronic components require thin films (qv), usually 5–50 μm deep, of materials. Amorphous thin films can be prepared by chemical vapor deposition, evaporation, and sputtering, in addition to the sol–gel process. In both evaporation and sputtering, the target is vaporized and redeposited onto a cold substrate. Vapor deposition can be carried out by using electron beams. It frequently results in porous films, and it can cause compositional changes in multicomponent glasses, because of differing vapor pressures at the deposition temperature. Vacuum evaporation can cause nonstoichiometry, but this problem can be alleviated for oxides by adding oxygen to the evaporation chamber. Sputtering is typically carried out by radio-frequency heating of argon gas to produce beams of argon ions that are directed at the sample. Some glasses prepared by thin-film techniques differ from bulk glasses in that they crystallize before reaching *T_g* (14).

Applications

Silicate glass is a familiar, ubiquitous material, used in beverage containers, window panes, and automobile windshields. Increasingly, however, unusual glasses are being employed in high technology applications.

Optical and Electrical Applications.

Optical Fibers for Telecommunications. There are several advantages in using light pulses through silica glass fibers for telecommunications (16). Signals sent through copper wires require repeaters or signal boosters at intervals of about 2 km; the repeaters in commercial fiber optic systems are 30 km apart (see FIBER OPTICS). Also, the glass fibers are so small (typically dia ~100 μm) that more of them fit into a cable of a given size. The glass fibers are not susceptible to electromagnetic interference, so the signal is clearer. Finally, the information carried on optical fibers can be modulated at very high frequencies, so many more simultaneous transmissions, eg, telephone conversations, are possible.

Communication by light rather than electricity required the development of suitable light sources as well as extremely pure, ultratransparent glass fibers. The use of long-wavelength radiation reduces intrinsic scattering from inhomogeneous density distributions, so infrared-transmitting fibers are desirable. The infrared light is usually produced by small semiconductor lasers (qv) or by light-emitting diodes (see LIGHT GENERATION). The fibers must be coated with a substance of lower refractive index in order to minimize losses. The fibers are also coated with a polymer immediately after drawing in order to prevent abrasion and hydroxyl formation at the surface. Fluorozirconate glasses transmit into the mid-ir, and they may be suitable for applications requiring relatively short lengths of fiber.

Graded-Refractive-Index Glasses. Light-focusing glass fibers and rods having radially parabolic refractive-index distributions are known as graded-refractive-index (GRIN) devices (18,19). These GRIN lenses can be made by ion-exchange (qv) techniques. In such a process, the glass is immersed in a bath of a suitable molten salt, and monovalent cations are replaced by other cations. Typically, nitrate or sulfate melts of lithium, potassium, or silver are used. GRIN glasses can also be made by chemical vapor deposition methods and by sol–gel processing. GRIN glasses are used as waveguides for coupling optical fibers and as lenses for compact photocopiers and compact disk players. The use of graded-refractive-index lenses could also reduce the number of elements needed in complicated optical systems such as cameras and microscopes.

Infrared Optics. Although the standard wavelength of transmission used in silica optical fiber networks is in the infrared (1.55 μm), there are applications in which glasses transmitting to longer wavelengths are preferable. These include nose cones for heat-seeking missiles; noninvasive monitoring of bodily fluids, eg, analysis of blood by transmitting ir radiation through an earlobe; and lenses for night vision equipment. Some chalcogenide and halide glasses transmit to the far-ir region (up to about 20 μm), but the relatively difficult preparation techniques and the relatively poor chemical, thermal, and mechanical properties of these glasses can complicate use. For example, some commercially available chalcogenide glasses must be sealed with a polymer coating to prevent slow reaction with air and water vapor.

Nonlinear Optical Glasses. Optoelectronic applications such as optical switches and modulators require materials having nonlinear optical (NLO) properties (see NONLINEAR OPTICAL MATERIALS) (20,21). Such properties are dependent on the square, cube, etc, of the intensity of the applied electric field and are noticeable only when high-energy sources such as lasers are used. It has been found that glasses containing small amounts of semiconducting microcrystals exhibit large optical nonlinearities (22,23). If the crystalline particles are less than about 5 to 10 nm in diameter, the movement of the charge carriers is greatly restricted, resulting in quantum confinement effects. Some examples of semiconductors where the quantum-dot effects in glass have been studied are CdS, CdSe, CuCl, and CuBr (22,23).

Acousto-Optic Glasses. In the acousto-optic effect, a surface acoustic wave (SAW) produced by transducers causes photoelastic index fluctuations that can diffract light. The SAW therefore acts as a traveling diffraction grating, and a guided optical wave is scattered by the SAW. The scanning of the scattered beam can be controlled by changing the frequency of the transducer drive signal. Chalcogenide glasses such as those in the Ge–As–S system have high indexes of refraction, low acoustical losses, and low sound velocities, making them candidates for acousto-optical applications. Acousto-optic microscanning devices could be used in laser printing, optical memory addressing, and information processing (24).

Fast-Ion-Conducting Glasses. One possible application of fast-ion-conducting glasses is in solid-state batteries (qv) for automobiles. The glasses might also be used in electrochromic displays or as sensors (qv) (25).

Glass–Ceramics. Glass–ceramic materials are first formed as glasses and then converted to polycrystalline ceramics by suitable heat treatments (26). The heat treatment schedule usually consists of a nucleation stage at lower temperatures, followed by a growth stage at higher temperatures. In general, glass-ceramics (qv) are stronger, harder, and more stable at high temperatures than are the parent glasses. One advantage of glass–ceramics over conventionally prepared ceramics is their fine-grained, nonporous, uniform structure. Another is the ability to form the parent glass into complex shapes before the crystallization occurs.

Glass Microspheres. It has long been known that plastics can be reinforced by the inclusion of glass fibers. A more recent development is the use of large amounts of small, hollow glass spheres as lightweight fillers to improve the mechanical properties of plastic insulators. High quality, hollow glass microspheres are also being used as containers for hydrogen (qv), deuterium, and tritium in inertial confinement nuclear fusion experiments (see FUSION ENERGY). Small glass beads containing short-lived radioactive elements can be injected into cancerous tumors, thereby providing higher and more localized doses of radiation (27).

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NONLINEAR OPTICAL AND ELECTROOPTIC CERAMICS

Nonlinear Optical Effects

When an intense beam of light from a laser (see LASERS) passes through certain transparent crystals, a portion of the beam emerges having a wavelength equal to half that of the incident beam. This effect, known as frequency doubling or second harmonic generation, takes place in a large number of crystalline materials at a wide range of wavelengths. The wavelength of the frequency-doubled beam depends on the incident wavelength and not the crystal used. The effect results from changes in the polarizability of the electrons in the crystal under the influence of intense light. In fact, in less intense optical fields, polarizability is constant giving rise to characteristic optical properties of materials such as the refractive index. Changes in polarizability constitute a nonlinear dependence of electronic polarization with light intensity, and this phenomenon is known as optical nonlinearity. Crystals that exhibit these effects are called nonlinear optical materials (qv).

Nonlinear optical (NLO) and electrooptic (EO) processes are events that take place in transparent materials where refractive indexes can vary with electric field intensity. The field elicits a polarization response in which terms dependent on second and higher orders of the field intensity become significant contributions to the overall polarization response. As light propagates through a transparent solid, liquid, or gas, it encounters the electric fields associated with the valence electrons, polarizing them and creating oscillating electric dipoles. These oscillators in turn act as antennas to broadcast or propagate the electric field through the medium. At low optical intensities, the polarizability P thus induced varies linearly with the electric field E :

$$P_i = \chi_{ij}^{(1)} E_j \tag{1}$$

where $\chi_{ij}^{(1)}$ is the linear polarizability. As electric field strength increases, eventually the polarization amplitude is no longer able to follow the electric field in a perfectly linear fashion. The polarizability, P_i , must now be expressed as a power series and the higher order terms become more significant with increasing field intensity:

$$P_i = \chi_{ij}^{(1)} E_j + \chi_{ijk}^{(2)} E_j E_k + \chi_{ijkl}^{(3)} E_j E_k E_l + \cdots \tag{2}$$

NLO effects result when the polarization response of the valence electrons becomes significantly anharmonic, usually in intense light beams where the magnitude of E is very large. The magnitudes of the coefficients of the terms in equation 2 diminish rapidly at higher orders, and thus readily observable NLO effects are either second-order ($\chi^{(2)}$) or third-order ($\chi^{(3)}$) processes. Most NLO applications rely on second-order processes. However, second-order processes generally occur only in crystalline materials that lack centers of inversion symmetry. Certain classes of materials such as piezo-, pyro-, and ferroelectric ceramics are noncentrosymmetric and are thus good candidates for use in constructing NLO devices. In fact, ferroelectric ceramics comprise the bulk of technologically useful nonlinear optical materials (see FERROELECTRICS).

NLO Wavemixing. Second harmonic generation (SHG) can be considered the mixing of two light waves of frequency ω to give a wave of frequency 2ω . It is also known as frequency doubling. This is readily accomplished by passing a beam of laser light through a NLO material appropriate for the wavelength and intensity of the beam. Sum-frequency generation (SFG) results when light waves of different frequencies mix to yield a wave where the frequency is the sum of those of the incident beams, and optical parametric oscillation (OPO) can be viewed as the disproportionation of a single beam into waves where frequencies add up to that of the original beam. These wavemixing processes can be highly efficient; for example, up to 70% of the energy from a 1064 nm Nd:YAG laser beam can be converted into 532 nm light by passing it through a crystal of potassium niobate [12030-85-2], KNbO₃, or potassium titanyl phosphate, KTiOPO₄.

Optical Phase Retardation. A static electric field applied to a ceramic changes its refractive indexes unequally, altering its birefringence, i.e., the difference between its minimum and maximum refractive indexes. This changes the polarization of a light beam transmitted through the crystal by altering the phase angle by which light polarized in the plane of the optic axis (the *e*-ray) leads or lags light polarized normal to the optic axis (the *o*-ray). Such an electrooptic (EO) device acts as a variable phase retarder, and can modulate either the frequency or the amplitude of a transmitted beam. Lithium niobate [12031-63-9], LiNbO₃, and lead lanthanum zirconate titanate (PLZT), (Pb,La)(Zr,Ti)O₃, are ceramic materials frequently used for EO applications.

Photorefractive Effect. In certain crystals, such as barium titanate [12047-27-7], BaTiO₃, and strontium barium niobate (SBN), Sr_{1-x}Ba_xNb₂O₆, applying a light pattern that causes alternate portions of the crystal to become illuminated or dark, eg, from the interference of two light beams, causes photoexcited charge carriers to drift from the illuminated to the dark regions, where they are trapped. This results in space charge fields in the crystal, which in turn causes adjacent zones to have different refractive indexes, setting up a diffraction grating within the crystal. Once written, this pattern can remain in the crystal for a considerable length of time until it is erased by strong, uniform illumination. This grating can diffract subsequent beams and is thus capable of storing, processing, and amplifying complex optical information such as images (see HOLOGRAPHY).

Materials and Processing

Materials. NLO materials possess a high degree of optical nonlinearity, physical durability and chemical inertness, and high threshold to optical damage. In addition, it must be possible to process the materials into the form required by the intended application.

Optically nonlinear ceramics all contain highly polarizable bonds. In the case of oxide ceramics, such polarizable bonds are often found between oxygen and early transition metals, eg, BaTiO₃, SrNb₂O₆, and KTaO₃; boron, eg, LiB₃O₅, β-BaB₂O₆; the heavy *p*-block elements, eg, TeO₂, HfO₂, Pb₃(PO₄)₂, and Bi₁₂SiO₂₀, and in compounds containing tetrahedral XO₄ groups, eg, KLiSO₄, KH₂PO₄, and Gd₂(MoO₄)₃. These compounds must crystallize in structures that favor highly directional bonding in order to yield good optical nonlinearities. For example, in LiNbO₃ the niobium atoms are not centrally located on six-coordinate (octahedral) positions but are off-center, rendering three niobium–oxygen bonds shorter than the others. The extra electron density within these short bonds causes them to become unusually polarizable. As in the bulk crystal, the polarizability of the Nb–O bonds contains higher order terms that result from anharmonicity in their electronic potentials. The first higher order term, β_{ijk} , is a microscopic susceptibility tensor that relates the second-order susceptibility of a bond or group to the bulk tensor $\chi_{ijk}^{(2)}$:

$$\chi_{ijk}^{(2)} = N G_{ijk} \beta_{ijk} \tag{3}$$

Here N is the number of bonds or molecules of a given type in the crystal, and G_{ijk} is a geometric tensor associated with a particular microscopic polarizability β ; this tensor is related to the crystallographic orientation of the bond. In extended systems such as covalent solids it becomes difficult to define a species to which one can assign a unique value of β , and thus the value of β for a given group can only be an approximate representation. In

lithium niobate the short, highly polarizable bonds align to give a nonzero value of $\beta_{\eta\hat{k}}$ for the NbO₄ group. The $\beta_{\eta\hat{k}}$ tensor is repeated in the same direction in each crystallographically equivalent group throughout the crystal, resulting in a large value of $\chi^{(2)}$. In contrast, the Ti atoms in cubic BaTiO₃ (T > 120 °C) are centered in their respective octahedral sites, and the polarizabilities of the Ti–O bonds yield a net value of zero for the $\beta_{\eta\hat{k}}$ terms of the TiO₆ groups.

Nonoxide NLO ceramics include Si and compound semiconductors (qv) having the silicon structure, eg, GaAs, InP, and InSb, as well as ferroelectrics such as SbSI. These materials tend to be more highly nonlinear than oxide ceramics, although lack of transparency at visible and uv wavelengths prevents them from competing with the oxides for the same applications.

Second-order nonlinearity in ceramics can also be seen as arising from a mixing of states in which the ground state can partially acquire the character of an excited state with a strong dipole moment, eg, a charge-transfer band or conduction band. The degree of optical nonlinearity that results depends on the extent to which the excited state is delocalized, as in the case of a conduction band, and the energy difference between the ground and excited states, that is, the band gap. Nonlinear susceptibilities of the best materials at a given wavelength tend to vary inversely with band gap.

NLO ceramics frequently used in the visible-near ir region generally crystallize in ferroelectric structure types, such as LiNbO₃ and the perovskite, eg, KNbO₃, BaTiO₃; tungsten bronze, eg, BaNa₂Nb₅O₁₅, Sr_{1-x}Ba_xNb₂O₇; KH₂PO₄; and KTiOPO₄ structures (see INFRARED AND RAMAN SPECTROSCOPY). Compounds with smaller nonlinearities but wider transparency regions include lithium borate, (LBO), LiB₃O₅, and β-barium borate (BBO), β-BaB₂O₄. The latter can frequency mix to wavelengths as short as 213 nm.

The physical durability of bulk ceramics and their resistance to chemical attack under ambient conditions allow device fabrication and use. Ceramics are generally resistant to optical damage, although damage thresholds can vary widely. Optical damage can result from thermal breakdown, in which prolonged illumination results in excessive heat build-up, usually in devices pumped by continuous-wave lasers, and avalanche breakdown, in which the electric field induced within the ceramic by the light beam exceeds the dielectric strength of the material, usually in high power pulsed-beam applications. Avalanche breakdown, which is often accompanied by a flash of broadband light resembling a spark, can cause dark inclusions to appear in the crystal. These introduce absorption and render the crystal more susceptible to further damage. Point defects such as vacancies and metal atom impurities in ceramics can lower the power threshold to avalanche breakdown, which in turn lowers the maximum useful laser power that may be safely used with the ceramic, limiting its efficiency.

Processing. All-optical wavemixing applications generally require single crystals. The crystals should have relatively low concentrations of point defects, which have been implicated in low thresholds to optical damage. Typical defects in ferroelectrics include Schottky defects and nonstoichiometry, which result in ions residing on the wrong crystallographic positions, eg, siting Nb on Li positions in LiNbO₃.

If the ceramic of interest melts congruently, eg, LiNbO₃ and BaTiO₃, crystals can be grown using the Czochralski method. In this technique a seed crystal suspended from a rotating mount is slowly withdrawn from a melt causing the material on the seed to crystallize as its temperature falls below the melting point. Eventually a large boule is pulled from the melt, from which crystals may be cut. If the ceramic melts incongruently, eg, KTiOPO₄, or is a phase not stable at the composition's melting point, eg, SiO₂, crystals may sometimes be grown hydrothermally, or from a nonaqueous flux.

In the flux-growth method, crystals of the desired ceramic are precipitated from a melt containing the components of the product phase, often in addition to additives used to suppress the melting point of the flux. These additives remain in solution after crystal growth is complete. Crystals are precipitated onto seeds by slowly cooling the melt or the seed, or occasionally by evaporating volatile components of the melt such as alkali halides, depressing the solubility of the product phase.

In the hydrothermal method, crystals of the desired ceramic are grown by dissolving the product or nutrient in the form of powder or small crystals in an aqueous solution of a mineralizer, which enhances the solubility of the nutrient. Examples of mineralizers include NaOH and K₂HPO₄, which aid the solution of SiO₂ (quartz) and KTiOPO₄, respectively. Crystal growth takes place in an autoclave that is heated above the critical temperature of water (374°C) and pressurized to maintain a density sufficient for adequate nutrient solubility. The disadvantages of greater equipment complexity and cost are often outweighed by the lower viscosity of the supercritical flux, which reduces flux inclusion, and lower growth temperatures that often yield lower defect concentrations.

Techniques and Applications

Frequency Conversion. SHG is most often used to double the frequencies of solid-state and diode lasers operating in the near infrared to yield an output beam in the visible spectrum. In this process laser light, frequently from a pulsed solid-state laser such as Nd:YAG, is directed through a doubling crystal such as LiB₃O₅ (LBO), KH₂PO₄ (KDP), etc in a direction that allows the output beam to remain in phase with the input beam. The emerging beam contains light at both the incident (fundamental) and second harmonic (SH) wavelengths. The extent to which light energy is converted to energy at this second harmonic (SH) frequency depends on the magnitudes of the coefficients of the $\chi^{(2)}$ tensor (eq. 2), as well as intensity of the fundamental beam. The chief material requirements for SHG are therefore high NLO coefficients and a high optical damage threshold. Other important criteria include optical transparency in the wavelength range of interest, and the ability to phase match the fundamental and SH beams. For phase matching to occur, there must be some angle of incidence through the crystal for which both the fundamental and second harmonic waves experience the same phase velocities, so that the velocity v_p of the SH wavevector k equals that of the fundamental wavevectors. Normal dispersion makes this a special condition: the crystal must be optically anisotropic, either uniaxial or biaxial, and the birefringence of the crystal must be such that the refractive indexes experienced by the interacting waves as they propagate through the medium match, ie $n(\omega) = n(2\omega)$, at some point on the surface of the refractive index ellipsoid (Fig. 1a). The refractive index ellipsoid defines n_i for a given polarization and crystallographic direction of propagation. If the refractive indexes do not match, the fundamental and SH beams cannot propagate in phase with one another. The distance the beams must propagate through the crystal to change the phase difference in the two beams is the coherence length l_c , which equals $\lambda / 4(n_{2\omega} - n_{\omega})$. The coherence length for a perfectly phase matched crystal is thus infinite.

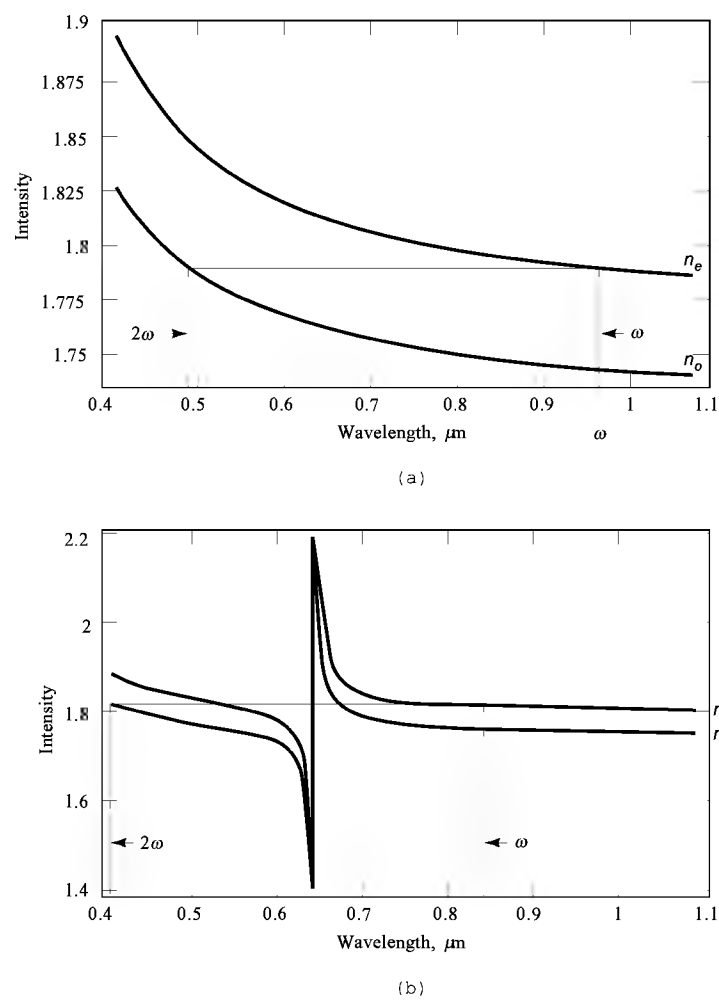


Fig. 1. (a) Phase matched second harmonic generation ($2\omega = 0.49 \mu\text{m}$) at $\omega = 0.98 \mu\text{m}$, where n_o refractive index by ordinary rays and n_e by extraordinary rays. (b) Hypothetical anomalous dispersion phase matching at 850 nm in similar a crystal having a Lorentzian absorption centered at 650 nm.

Biaxial crystals offer the possibility of coincidence of the phase matching direction with one of the optic axes. This highly desirable situation, called non-critical phase matching, is quite tolerant of divergence of the incident beam from the most efficient phase matching direction.

Anomalous dispersion offers another method of phase matching. Anomalous dispersion, the opposite of normal dispersion, refers to a decrease in refractive index with decreasing wavelength and is associated with optical absorption. The magnitude of anomalous dispersion depends on the width and intensity of the absorption band. In principle, it is possible to introduce absorption between fundamental and SH wavelengths to reduce or overcome normal dispersion, allowing phase matching to take place in a weakly birefringent crystal (Fig. 1b). As of this writing, anomalous dispersion-assisted phase matching has not been demonstrated in inorganic crystals.

The range of useful SHG wavelengths for a given material is usually marked by the limits of its phase matching ability, as this window is usually narrower than its transparency range. Phase matching ranges and NLO coefficients for some of the more familiar NLO materials are given in Figure 2.

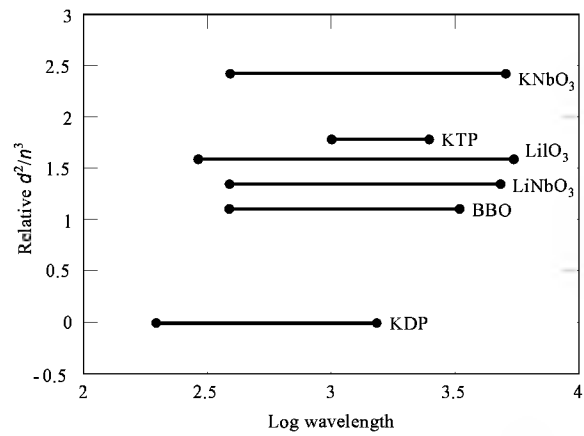


Fig. 2. Optical nonlinearity and phase matching windows for commonly used NLO materials. KDP = KH_2PO_4 ; BBO = $\beta - \text{BaB}_2\text{O}_4$; KTP = KTiOPO_4 . Wavelength is in units of nm. d^2/n^3 = normalized second order susceptibility with refractive index.

SH light can be used to pump a second NLO crystal to generate light at one-third the wavelength of the fundamental (cascade tripling) through sum-frequency generation (SFG), to yield a wavelength-tunable output beam through optical parametric oscillation (OPO), to drive a dye laser or Raman shifter, or in optical data storage (see INFORMATION STORAGE MATERIALS).

Electrooptic Devices. Electrooptic (EO) materials are optical media in which birefringence can be readily induced or altered by an externally applied electric field. Birefringence, which is the difference between minimum and maximum refractive index (Δn) in an optical medium, occurs in anisotropic crystals, stressed glasses, poled ceramics, or any transparent medium subjected to an external electric field. If linearly polarized light enters a birefringent material normal to its optic axis, the maximum attenuation obtained from an analyzer is found when the analyzer is offset from 90° by a certain phase retardation angle. This phase retardation angle depends on the birefringence and thickness of the element, and on the wavelength of light being transmitted.

The incident beam is broken up into an ordinary ray (*o*-ray) polarized normal to the optic axis, and an extraordinary ray (*e*-ray) polarized in the plane of the optic axis. The extraordinary ray is so named because unlike the ordinary ray, it does not obey Snell's law of refraction. The *o*-ray and the *e*-ray experience different refractive indexes and therefore different phase velocities. Either the *o*-ray or the *e*-ray lags behind the other in phase and the emerging beam is elliptically polarized. The sign of the birefringence determines which ray is retarded: in a positive uniaxial crystal, the optic axis is a fast axis and the *o*-ray leads in phase; conversely, if the birefringence is negative the optic axis is the slow axis and the *o*-ray lags behind the *e*-ray. The phase retardation Γ experienced by the light beam on passing through the optical element is defined as

$$\Gamma = \frac{2\pi L}{\lambda} (n_o - n_e) \tag{4}$$

where L is the optical path length, n_o and n_e are the refractive indexes experienced by the *o*-ray and *e* ray, and λ is the wavelength of the incident beam. If $\Gamma = \pi/2$ the emerging beam is circularly polarized and the element is a quarter-wave plate. If $\Gamma = \pi$, the beam is linearly polarized orthogonally to the polarization of the incident beam, and the element is a half-wave plate. If such a device is placed between two crossed polarizers and rotated, the relative intensity I/I₀ of light transmitted through this device varies as $\sin^2(\Gamma/2)$.

In an electrooptic material the phase retardation angle is controlled by altering birefringence, which is in turn controlled by the potential of an applied electric field. An electrooptic device thus acts as a variable phase optical retardation plate, and can be used to modulate the wavelength or intensity of an incident beam.

EO effects can be linear or quadratic, depending on whether the degree of phase retardation varies with either the first or second power of applied voltage. The variation of birefringence with potential takes the form

$$r_c = -(2\Delta n) - n^3 E \tag{5}$$

where r_c is the linear, or Pockels, coefficient and

$$R = -(2\Delta n) - n^3 E^2 \tag{6}$$

where R is the quadratic or Kerr coefficient. As is the case with second-order NLO materials, phases demonstrating the Pockels effect are noncentrosymmetric, though no such constraint is placed on materials demonstrating the Kerr effect. In general, large values of r_c and R for a given material correlate with increased $\chi^{(2)}$ and $\chi^{(3)}$ effects at optical frequencies.

As with NLO ceramics, good EO materials tend to be ferroelectrics. Ferroelectric materials are noncentrosymmetric, allowing one to take advantage of the linear response and increased magnitude of the Pockels effect vs the Kerr effect. Also, the large low frequency dielectric constants typical of many ferroelectric ceramics are conducive to high values of r_c , although larger dielectric constants necessitate a higher driving voltage to achieve a given response. EO ceramics are also frequently based on perovskite and tungsten bronze structures containing Nb and Ti, and include LiNbO₃, PbZr_{1-x}Ti_xO₃ (PZT), KTiOPO₄, Sr_{1-x}Ba_xNb₂O₇, Ba₂NaNb₅O₁₅, and BaTiO₃.

Inorganic electrooptic materials can take the form of single crystals or polycrystalline ceramics. For certain applications such as switching and interferometry, single crystals carry certain advantages over polycrystalline compacts. On the other hand, polycrystalline ceramics can be hot-pressed or sintered into a larger variety of shapes and sizes, without regard to crystallographic orientation. In addition, the orientation of the optic axis in such polycrystalline ceramic elements can be controlled by the external electric field. It should be noted that operations making use of properties that depend on crystallographic orientation, such as SHG, would be difficult to accomplish with pressed ceramics consisting of randomly oriented crystallites.

EO materials are generally used as either bulk optical elements or guided wave devices. Bulk elements are frequently made of polycrystalline ceramics such as lead lanthanum zirconate titanate (PLZT), (Pb,La)(Zr,Ti)O₃, whereas guided wave devices are usually fabricated on single crystals of materials such as LiNbO₃ and KTiOPO₄. Bulk elements are used where significant apertures are required and large modulator bandwidths are less important, and are used in devices such as variable density filters, variable color filters, electrooptic shutters, and as Q-switches for pulsed lasers. The Q-switch takes advantage of the fast response time of the EO material, admitting a single laser pulse by switching between on and off states in less than 1 ns. Guided wave devices are used as signal modulators and as interferometers. A simple example of such a device is a single channel phase modulator, which alters the phase retardation of a beam propagating through the waveguide. A difference in refractive index between the waveguide and the remainder of the crystal keeps the light beam from escaping the channel. This refractive index gradient is created by replacing metal ions in the crystal with foreign ions through diffusion, eg Ti for Nb in LiNbO₃ and Tl for K in KTiOPO₄. Such an element can be used to modulate optical phase at very high frequencies, allowing high bandwidth signal transmission through fiber optic cables.

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ELECTRONIC PROPERTIES AND MATERIAL STRUCTURE

The properties of a ceramic material that make it suitable for a given electronic application are intimately related to such physical properties as crystal structure, crystallographic defects, grain boundaries, domain structure, microstructure, and macrostructure. The development of ceramics that possess desirable electronic properties requires an understanding of the relationship between material structural characteristics and electronic properties and how processing conditions may be manipulated to control structural features.

Properties and Applications

Insulators. Ceramic insulators are materials used to support electrical conductors and to prevent the flow of electrical charge between them. Ceramic bodies, such as triaxial porcelains based on compositions in the $\text{Al}_2\text{O}_3\text{--}(\text{K},\text{Na})_2\text{O--SiO}_2$ phase diagram, were initially employed as high voltage insulators. Since then, other ceramics have been utilized in higher technology insulation applications, eg, in packaging and very large-scale integration (VLSI) circuits (see INTEGRATED CIRCUITS). VLSI, or multilayer ceramic (MLC), technology involves cofiring conductor and insulator layers to build-up multilayer electronic modules, thus increasing device, or circuit, density. Alumina, Al_2O_3 , is the material most frequently used for these applications, although because of its very high thermal conductivity, beryllia, BeO , has also been used as a substrate material. Other ceramics, namely, aluminum nitride and glass-ceramics (qv), such as cordierite [12182-53-5] and cordierite–mullite composites, have also been investigated for use in packaging applications (see PACKAGING, SEMICONDUCTORS AND ELECTRONIC MATERIALS). The development of cordierite as a substrate material has progressed to the state where, in conjunction with cosinterable copper electrodes, it is used as the multilayer substrate in high performance computers (see COMPUTER TECHNOLOGY).

The usefulness of ceramics for all of these applications is because of their dielectric, or insulating, characteristics. Properties important for insulation applications include: (1) dielectric constant k' : a measure of the ability of a material to store electrical charge; (2) electrical resistivity ρ : the resistance to current flow; (3) dissipation factor or $\tan \delta$; a measure of the energy loss per cycle (in an a-c field); and (4) dielectric breakdown strength (DS): the maximum voltage gradient that can be impressed across the dielectric without destroying its insulating characteristics. So that dielectric loss may be minimized, materials having low (<10) dielectric constants and low (<0.001) dissipation factors are desired for substrate applications.

The observed dielectric constant k' and the dielectric loss factor $k'' = k' \tan \delta$ are defined by the charge displacement characteristics of the ceramic; ie, the movement of charged species within the material in response to the applied electric field. Discussion of polarization mechanisms is available (1).

Other features of ceramic materials are also important in insulation applications. For example, in packaging applications, not only the electrical properties of Al_2O_3 , but also the thermal conductivity, for heat dissipation, thermal expansion behavior, and mechanical strength are important. Properties of ceramic insulators are affected by the composition and processing history of the ceramic body. For example, for triaxial porcelains processed by viscous sintering, the relative amounts of the raw materials used, kaolin and ball clay (primarily $\text{Al}_2\text{O}_3 \cdot 2\text{SiO}_2 \cdot 2\text{H}_2\text{O}$) (see CLAYS); feldspar, $(\text{K},\text{Na})_2\text{O} \cdot \text{Al}_2\text{O}_3 \cdot 6\text{SiO}_2$; and flint, SiO_2 ; and the time—temperature processing cycle, determine the relative amounts of the resulting phases (mullite, alkali-silica glass, and silica) present.

In contrast to triaxial porcelains, packaging materials such as 99% Al_2O_3 prepared by a solid-state sintering process, display significantly lower dielectric loss. In these materials, there is no residual glassy phase with its associated mobile ion content, and therefore, conduction losses are minimized.

Capacitors. Ceramic materials suitable for capacitor (charge storage) use are also dependent on the dielectric properties of the material. Frequently the goal of ceramic capacitors is to achieve maximum capacitance in minimum volume. The defining equation for capacitance is given by:

$$C = k' \epsilon_0 \frac{A}{d}$$

(1)

where k' is the dielectric constant, ϵ_0 is the permittivity of free space, A is the electrode area, and d is the separation between the electrodes. Whereas the dielectric constant is a fundamental material property, it depends on such factors as temperature, stress, electric field strength, and measurement, or use, frequency. Physical features of the ceramic, such as porosity, grain size, and the presence of grain boundary phases, may also affect the observed dielectric constant. The charge storage capabilities of ceramic capacitors are increased by: (1) using ferroelectric or relaxor ferroelectric materials (see FERROELECTRICS); (2) preparing materials having large effective dielectric constants ($k' \sim 10,000\text{--}60,000$) through control of the electric susceptibilities and resistivities of grain and grain boundary phases, eg, internal boundary layer capacitors (IBLCs); or (3) using a multilayering approach, to prepare a structure having alternating electrode–dielectric layers.

Historically, materials based on doped barium titanate were used to achieve dielectric constants as high as 2,000 to 10,000. The high dielectric constants result from ionic polarization and the stress enhancement of k' associated with the fine-grain size of the material. The specific dielectric properties are obtained through compositional modifications, ie, the inclusion of various additives at different doping levels. For example, additions of strontium titanate to barium titanate shift the Curie point, the temperature at which the ferroelectric to paraelectric phase transition occurs and the maximum dielectric constant is typically observed, to lower temperature as shown in Figure 1 (2).

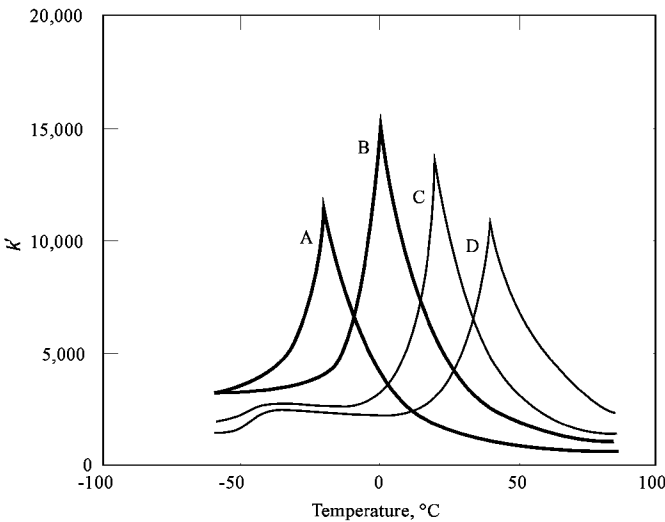


Fig. 1. Effect of compositional variations on the dielectric properties of strontium titanate-barium titanate solid solutions. A, $\text{Ba}_{0.1}\text{Sr}_{0.9}\text{TiO}_3$; B, $\text{Ba}_{0.8}\text{Sr}_{0.2}\text{TiO}_3$; C, $\text{Ba}_{0.74}\text{Sr}_{0.26}\text{TiO}_3$; and D, $\text{Ba}_{0.79}\text{Sr}_{0.21}\text{TiO}_3$ (2).

Because of very high dielectric constants ($k' > 20,000$), lead-based relaxor ferroelectrics, $\text{Pb}(\text{B}_1\text{B}_2)\text{O}_3$, where B_1 is typically a low valence cation and B_2 is a high valence cation, have been investigated for multilayer capacitor applications. Relaxor ferroelectrics are dielectric materials that display frequency dependent dielectric constant versus temperature behavior near the Curie transition. Dielectric properties result from the compositional disorder in the B_1 and B_2 cation distribution and the associated dipolar and ferroelectric polarization mechanisms. Close control of the processing conditions is required for property optimization. Capacitor compositions are often based on lead magnesium niobate (PMN), $\text{Pb}(\text{Mg}_{1/3}\text{Nb}_{2/3})\text{O}_3$, and lead zinc niobate (PZN), $\text{Pb}(\text{Zn}_{1/3}\text{Nb}_{2/3})\text{O}_3$.

Multilayer capacitor devices have become progressively smaller as the dielectric constant of the ceramic layers has increased, and layer thickness has decreased to below 15 μm . The gain in volumetric efficiency over a standard single-layer, or disk, capacitor ($C \propto \epsilon \propto k' \propto \mu\text{F cm}^{-3}$) may be estimated by assuming a typical multilayer capacitor configuration (50, 15- μm thick, 0.25 cm^2 area dielectric layers having $k' \approx 10,000$). Using these assumptions, a volumetric efficiency of 230 $\mu\text{F cm}^{-3}$, or a two-order of magnitude gain in efficiency, is observed. In addition to high volumetric efficiency, these devices also offer high reliability, low cost, and large absolute capacitance.

There is also growing interest in thin-film dielectric capacitors. For example, through the use of processing techniques such as sol-gel solution deposition, thin ($\sim 0.25 \mu\text{m}$) ceramic layers having dielectric constants ranging from 500 to 2000 in the PZT, $\text{Pb}(\text{Zr,Ti})\text{O}_3$, and PMN-PT, $\text{Pb}(\text{Mn}_{1/3}\text{Nb}_{2/3})\text{O}_3$ - PbTiO_3 , compositional families respectively, have been prepared (3).

Piezoelectrics. All ceramics display a slight change in dimension, or strain, under the application of an electric field. When the induced strain is proportional to the square of the field intensity, it is known as the electrostrictive effect, and is expressed by:

$$S = \xi E^2 \tag{2}$$

where ξ is the electrostrictive coefficient ($\text{m}^2 \text{V}^{-2}$) and E is the applied electric field (V m^{-1}). Materials that also show the opposite effect, ie, an induced polarization (electric charge) resulting from an applied stress, are referred to as piezoelectric materials, and the effect is referred to as the direct piezoelectric effect. Piezoelectric properties may be described in terms of D , the dielectric displacement; E , the electric field; and T , the applied stress. The direct piezoelectric effect is expressed by:

$$D = dT \tag{3}$$

where d is the direct piezoelectric coupling coefficient expressed in C N^{-1} . Piezoelectric materials also display the reverse effect; ie, the development of a strain S in response to an applied electric field (the converse piezoelectric effect):

$$S = d^* E \tag{4}$$

where d^* is the converse piezoelectric coupling coefficient, expressed in m V^{-1} . Generally, the first-order piezoelectric coupling coefficient is much larger than the second-order electrostrictive coefficient, and therefore, for the applications discussed, the piezoelectric response of the material is more important than the electrostrictive response. Although not indicated in the above equations, ξ , d , and d^* are all tensor material properties, and thus are directional in nature.

Certain crystal symmetry requirements are necessary for the existence of piezoelectric behavior in materials. The most widely used class of piezoelectric ceramics possess the ABO_3 perovskite crystal structure, where A is usually a low valence cation and B is a high valence cation. The structure consists of a cubic close packed array of oxygen and A-site ions, and the B-site ions occupy one-fourth of the octahedral interstices that are not adjacent to the A-site ions. Other useful piezoelectrics possess the tungsten bronze, AB_2O_6 , structure.

The piezoelectric electromechanical coupling effects allow for the conversion of mechanical energy into electrical energy or electrical into mechanical energy, thus defining two different classes of transducer applications. Uses range from hydrophones and microphones, to power transducers for ultrasonic cleaning baths. Other applications include filters and resonators. Most (polycrystalline) piezoelectric ceramics for transducer applications are based on compositions in the PZT, PbZrO_3 - PbTiO_3 , family. The materials are used in a polycrystalline form, and to observe the piezoelectric effect, the bulk ceramic must first be uniformly polarized. This is typically accomplished by taking advantage of the ferroelectric nature of PZT and poling after processing (4). PZT compositions near the morphotropic phase boundary are frequently selected not only because they possess high piezoelectric coupling coefficients, but because they are also more easily poled. Other piezoelectric materials that have been employed include quartz, doped BaTiO_3 , doped PbTiO_3 , which has been used for acoustic imaging, and PZT-polymer composites, which have been used in hydrophone applications.

Pyroelectrics. Pyroelectric ceramics are materials that possess a unique polar axis and are spontaneously polarized in the absence of an electric field. Pyroelectrics are also a subset of piezoelectric materials. Ten of the 20 crystal classes of materials that display the piezoelectric effect also possess a unique polar axis, and thus exhibit pyroelectricity. In addition to the induced charge resulting from the direct pyroelectric effect, a change in temperature also induces a surface charge (polarization) from the piezoelectric nature of the material, and the strain resulting from thermal expansion.

Ceramics that display the pyroelectric effect also exhibit a variation in polarization with temperature, as shown in Figure 2. The nature of the temperature variation is dependent on the type of crystallographic transformation that the material displays at the Curie point; ie, whether the transition is first or second order.

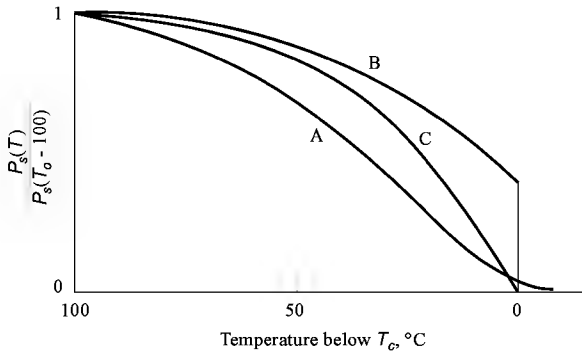


Fig. 2. Polarization plotted as a function of temperature below the Curie transition temperature T_c for A, relaxors; B, first-order; and C, second-order ferroelectrics (5).

The most commercially important application that takes advantage of the pyroelectric effect in polycrystalline ceramics is infrared detection, especially for wavelengths in excess of 2.5 μm . Applications range from radiometry and surveillance to thermal imaging, and pyroelectric materials work under ambient conditions, unlike photon detectors, which require cooling.

A second mode of pyroelectric operation is also possible. In addition to the standard pyroelectric mode, where a change in the detector temperature caused by a variation in the incident radiation intensity results in a change in polarization and therefore a current flow as described herein, ferroelectric ceramics may also be operated in a dielectric bolometer mode. Operation in this mode is based on the variation in permittivity ($d\epsilon/dT$) that occurs in the region of the Curie transition (Fig. 3). A change in the detector temperature, arising from a change in the incident radiation level, causes a variation in the permittivity, and when the detector is operated under an applied bias, a voltage output results.

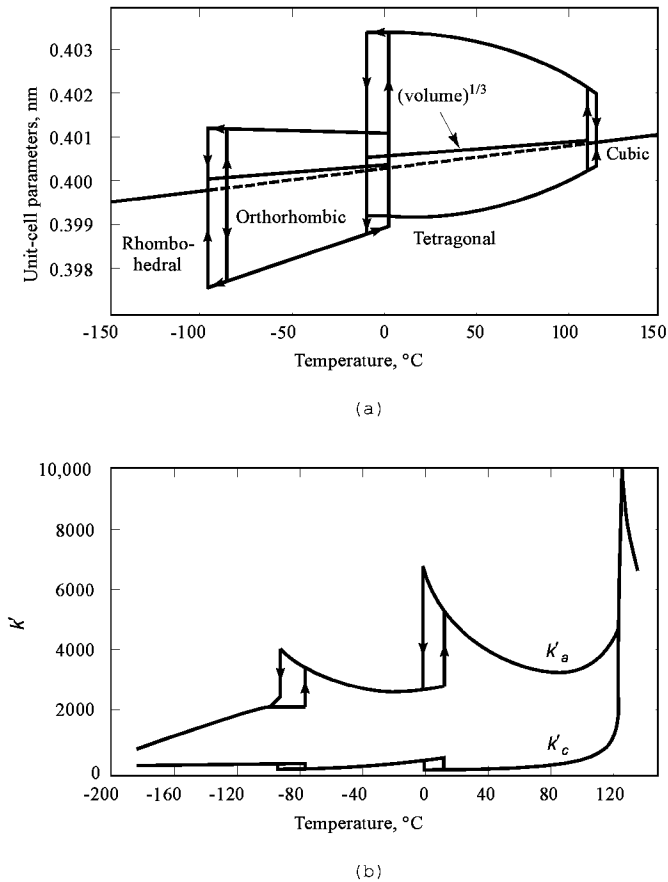


Fig. 3. (a) Crystallographic and (b) dielectric properties of BaTiO₃ as a function of temperature (6,7).

The perovskite ferroelectrics are again the most frequently used ceramics for infrared detector applications. Both single-crystal and polycrystalline materials have been investigated. Single-crystal lithium tantalate, LiTaO₃, has been used in single-element detectors. Polycrystalline ceramic devices are frequently based on lead scandium tantalate (for bolometer mode operation), or other lead-based ABO₃ perovskite compositions. Various dopants are added to optimize specific properties, such as pyroelectric coefficient, the Curie transition temperature, permittivity, and dielectric loss. The detector element compositions can become fairly complex with the inclusion of these additives. For example, one material (8) is based on lead zirconium iron niobate (PZFN), but also incorporates titanium and uranium additions to improve the properties, resulting in the following composition: Pb_{1.02}(Zr_{0.58}Fe_{0.20}Nb_{0.20}Ti_{0.02})_{0.994}U_{0.00}O₃. The small amount of excess lead is added to improve the sintering behavior of the material.

Single-crystal pyroelectrics are generally prepared by Czochralski growth. Polycrystalline materials are frequently prepared by hot pressing, followed by subsequent thinning and polishing to prepare sections ~10–30 μm in thickness. Multielement arrays are prepared from these sections by selective etching, electroding, and connection to silicon microcircuitry using solder-bump technology. Developments in the sol-gel processing of ferroelectric thin films and sacrificial etching techniques may allow for more straightforward, direct integration of pyroelectric detectors onto silicon devices.

Ferroelectrics. Ferroelectrics, materials that display a spontaneous polarization in the absence of an applied electric field, also display pyroelectric and piezoelectric behavior. The distinguishing characteristic of ferroelectrics, however, is that the spontaneous polarization must be re-orientable with the application of an electric field of a magnitude lower than the dielectric breakdown strength of the material.

The ferroelectric properties of perovskite materials, and the onset of ferroelectric behavior at a specific temperature, are inherently related to both the domain and crystal structures of the material. For example, in ABO₃ perovskite ferroelectrics, the onset of a macroscopic spontaneous polarization, ie, the spontaneous alignment of dipoles, that is observed on cooling below the Curie temperature is intimately related to a change in the crystal structure occurring at the Curie temperature. As an example, BaTiO₃ transforms on cooling from a cubic paraelectric structure to a tetragonal ferroelectric structure at a T_c of ~125 °C. This crystallographic distortion involves ionic displacements that destroy the symmetry of the nonpolar structure, and includes movement of the B-site species to minimum free energy, off-center positions resulting in the generation of permanent electric dipoles in the material, the observed macroscopic spontaneous polarization, and the comparatively high dielectric constants associated with dipolar polarization. Crystallographic and dielectric properties of BaTiO₃ are shown in Figure 3.

The number of applications utilizing the ferroelectric response of ceramic materials has been limited. Memory products are under development and are anticipated to be commercially available during the early to mid-1990s.

Ferrites. Magnetic ceramics or ferrites (qv) may be classified according to crystal structure and the type of magnetic properties: (1) spinel ferrites; (2) hexagonal ferrites, ie, the magnetoplumbites; and (3) rare-earth ferrites, which crystallize in the garnet structure. The garnet materials, so named because they crystallize in the structure of garnet, have the chemical formula 3Me₂O₃·5Fe₂O₃, where Me is Y or Gd. These rare-earth ferrites are used in microwave devices (see MICROWAVE TECHNOLOGY) and bubble memory applications.

Hard materials, so named because they are difficult to demagnetize, are used in permanent magnet applications. The general chemical formula for these materials is MeO·6Fe₂O₃, where Me is a Group 2 (IIA) metal, usually Sr or Ba. The materials crystallize in a hexagonal structure, leading to the name hexagonal ferrites or hexaferrites. They are also isostructural with the naturally occurring mineral, magnetoplumbite.

The most commonly used ferrites, the so-called soft ferrites, are used in soft magnet and low field telecommunication applications, low power

transformers, television tube scanning yokes, recording heads, magnetic recording media (see MAGNETIC TAPE), antennae, and channel filters. Soft ferrites crystallize in the spinel structure and are characterized by the general formula, MeFe_2O_4 . That is, they consist of a divalent oxide, MeO , typically a transition-metal oxide, such as NiO , CoO , MnO , or ZnO , and iron oxide, Fe_2O_3 . The spinel crystal structure is a cubic AB_2O_4 structure, named for the naturally occurring mineral spinel, MgAl_2O_4 . It consists of cubic close-packed oxygen ions with one-eighth of the tetrahedral sites occupied by divalent Mg , and one-half of the octahedral sites occupied by trivalent Al . Some ferrites also crystallize in the inverse spinel structure, where the divalent cations reside on the B sites, and the trivalent cations are equally split between the A and B sites. Other ferrites, such as MnFe_2O_4 , have an intermediate structure, with ~80% of the manganese ions on the A site and the remaining 20% on the B site. The ferromagnetism of the soft ferrites results from the antiferromagnetic coupling between the cations on the two different crystallographic sublattices.

The existence of solid solutions between different mixed oxides allows for a substantial ability to tailor specific properties. The most common of the soft ferrites is manganese zinc ferrite, $\text{MnFe}_2\text{O}_4\text{--ZnFe}_2\text{O}_4$, and the ability to tailor properties in this system results, in part, from the fact that manganese is paramagnetic whereas zinc is nonmagnetic. A typical ferrite composition also includes other oxide dopants, such as calcia and silica. During processing, these dopants migrate to the grain boundaries, which increases the resistivity of the ferrite, and further minimizes eddy current loss. Because eddy current loss is inversely proportional to frequency, ferrites are well suited to high frequency applications. Other properties that may be tailored through compositional control include coercivity, saturation flux density, and permeability (9).

Sensors. One growth area for electronic ceramics is in sensor applications. Sensors (qv) are devices that transform nonelectrical inputs into electrical outputs, thus providing environmental feedback. Smart, or intelligent, sensors also allow for mechanisms such as self-diagnosis, recovery, and adjustment for process monitoring and control (see PROCESS CONTROL).

Ceramic sensor applications are widely varied and likely to grow in part, because of the increasing emphasis on process control, waste minimization, and environmentally conscious manufacturing. Sensors are used for the measurement of humidity, oxygen gas pressure, carbon monoxide concentration, pressure, temperature, radiation, etc. For example, some humidity sensors are dependent on the p/n junction characteristics of a NiO--ZnO interface; oxygen gas sensors on the electronic conductivity properties of ZrO_2 ceramics; pressure sensors on the bulk piezoelectric properties of PZT ceramics (see PRESSURE MEASUREMENTS); and temperature sensors on the grain boundary characteristics of doped BaTiO_3 ceramics (see TEMPERATURE MEASUREMENTS).

The performance characteristics of ceramic sensors are defined by one or more of the following material properties: bulk, grain boundary, interface, or surface. Sensor response arises from the nonelectrical input because the environmental variable effects charge generation and transport in the sensor material.

Typical positive temperature coefficient (PTC) device behavior for a doped polycrystalline BaTiO_3 thermistor is presented in Figure 4. At temperatures below ~100°C and above ~200°C the material shows the expected negative resistivity vs temperature associated with semiconductors as expressed by:

$$\rho(T) = \rho_o \exp\left(\frac{E_a}{kT}\right)$$

(5)

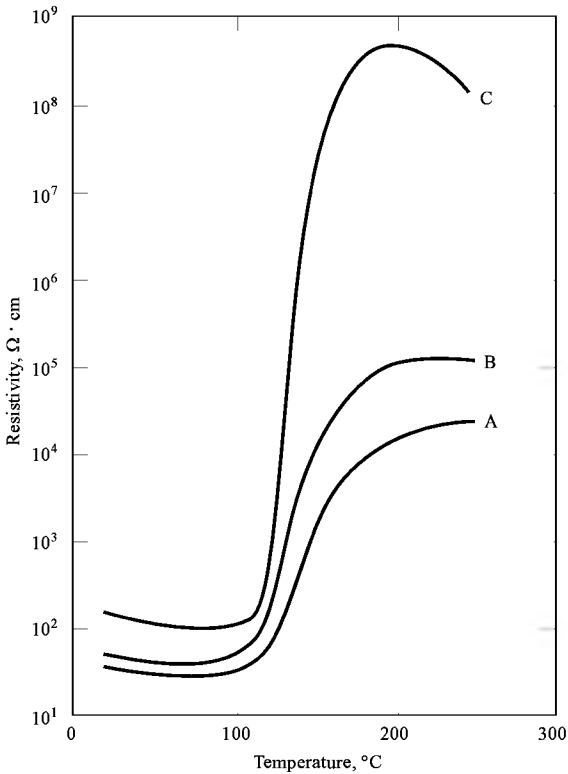


Fig. 4. Effect of dopant additions on the resistivity versus temperature behavior of BaTiO_3 PTCR ceramics. A, undoped; B, doped with 0.134 mol % Cr; and C, doped with 0.127 mol % Mn.

where $\rho(T)$ is the resistivity at temperature, T ; ρ_o is the pre-exponential factor; E_a is the activation energy for conduction; and k is the Boltzmann constant. This equation describes the thermal generation of carriers, or the increase in carrier mobility, which occurs over the temperature ranges where bulk transport phenomena control conductivity. At temperatures between about 100 and 200°C, however, the resistivity increases by several orders of magnitude.

Because PTC thermistor compositions are generally processed under either reducing atmospheres or using La^{3+} or Y^{3+} (for Ba) dopant additions, donor states are generated in the grains, and these become semiconducting. At the grain boundaries acceptor states are formed through either acceptor impurity (Mn, Cr) segregation or chemisorption of oxygen during the annealing or cooling phase of the process cycle. This results in the formation of a potential barrier at the grain boundary. This barrier height increases with temperature above the Curie-Weiss temperature, and the increase in resistance, ie, the PTC effect, results. Because the acceptor doping level can affect the barrier height, the magnitude of the resistance increase that is observed in the vicinity of the Curie temperature can be controlled by dopant, as shown in Figure 4.

Varistors. Varistors are devices that exhibit nonlinear current–voltage behavior. At low voltages, current flow is minimal and the device behaves as an ohmic insulator. As the voltage approaches a critical value, the breakdown field (F_{BR}), current flow increases and the device becomes highly

conducting. Because of this characteristic, varistors are typically employed as circuit overvoltage protection devices, ie, devices that protect solid-state circuitry and other components against voltage spikes by diverting the current flow. The most frequently used material is doped zinc oxide, ZnO, which can handle both high current and high energy. Dopants include Sb₂O₃, Bi₂O₃, CoO, MnO, and Cr₂O₃, present in quantities of <1 mol %. A typical composition is 96.5ZnO–0.5Bi₂O₃–1.0CoO–0.5MnO–1.0Sb₂O₃–0.5 Cr₂O₃.

Standard ceramic processing conditions are controlled so that the resulting ceramic microstructure is composed of semiconducting zinc oxide grains ($\rho_{ZnO} < 1\Omega\text{cm}$) and electrically insulating grain boundaries ($(\rho_{gb} > 10^6\text{ }\Omega\text{cm})$). The microstructure is thus similar to that of the BaTiO₃ thermistor and device performance is dependent on the characteristics of the electrically insulating barriers at the grain boundaries, which result from trap states associated with the dopants (5,10).

High Temperature Ceramic Superconductors. In 1986, it was reported that the compound (La, Ba)₂CuO₄ displayed the transition to the superconducting state at a temperature of ~35 K. To be superconducting, a material must display two effects. First, it must display the Meissner effect at temperatures below T_c , the superconducting transition temperature. That is, the material must become diamagnetic and expel an externally applied magnetic field. Second, the electrical resistivity must decrease to zero at temperatures below T_c .

This extraordinary discovery of superconductivity in a ceramic material led to an explosion of research on other ceramic systems. The most notable include: YBa₂Cu₃O_{7-δ}, $T_c \sim 93\text{ K}$; Bi₂CaSr₂Cu₂O₈, $T_c \sim 80\text{ K}$; and Tl₂Ca₂Ba₂Cu₃O₈, $T_c \sim 125\text{ K}$. Other bismuth- and thallium-based superconductors having different cation stoichiometries have also been discovered. The observed electrical properties of this family of ceramics are dependent on the crystallographic features and defect chemistry oxygen stoichiometry of the materials (11). Because the superconducting properties of these compounds are a function of their oxygen content, a key aspect to processing is control of the oxygen partial pressure during heat treatment.

Ceramic, or oxide, superconductors (powders, thin films, and single crystals) have been prepared by a variety of techniques. Superconducting powders have been prepared by both traditional mixed oxide and chemical coprecipitation methods. The powders are processed into the desired form by techniques such as extrusion, pressing, or isostatic pressing. Thin films of the oxide superconductors have been prepared by a variety of sputtering techniques and chemical solution deposition approaches. Epitaxial growth and orientation of the films have been observed, and the fabrication of weak link Josephson junctions suitable for superconducting quantum interference devices (SQUIDs) has been reported (12). Finally, reasonably large single crystals of these materials have also been prepared. One technique that has been used extensively is flux growth, ie, growth from a molten salt bath.

Processing Techniques

Traditional Processing Routes. The majority of the electronic ceramics that are used for electronic applications crystallize in the perovskite structure. Many perovskite-type oxides can be prepared by conventional processing routes, ie, by high temperature solid-state reactions between the respective oxide powders. For example, to prepare the ABO₃ perovskite PZT, PbO, ZrO₂, and TiO₂ are calcined at temperatures of ~900° C to induce crystallization into the desired structure. In addition to oxide precursors, carbonate powders of fine size may also be used to improve reaction kinetics and ensure a more complete reaction. For this process it is essential to remove the potential carbon contaminants during subsequent heat treatment. For materials having volatile constituents, such as the lead-based perovskite materials, additional measures are required to suppress, or compensate for, lead volatility during heat treatment. These include adding excess lead oxide to the initial batch, and or carrying out the calcination and sintering operations in a lead-rich atmosphere. Although processing to net-shape or near net-shape is desirable, a final machining step to yield a part of the exact size required is often necessary.

Chemical Coprecipitation of Powders. In the preparation of ceramics for such applications as piezoelectric transducers, traditional mixed oxide processing routes yield materials having acceptable properties. However, for the production of electrooptic ceramic components, deficiencies in the chemical homogeneity and optical properties prepared by these methods are frequently evident. Thus chemical methods of preparation, especially that of coprecipitation, are used to prepare powders for high quality defect-free optical devices. Because chemical methods of preparation are more costly than mixed oxide methods, the device requirements must necessitate the use of the more expensive processing techniques. Coprecipitation methods have been used extensively for the preparation of barium titanate, lanthanum-doped lead zirconate titanate (PLZT), and oxide superconductor powders.

In general, solution-based preparation methods involve dissolving precursor salts of the desired product, such as nitrates or chlorides, in a solvent, and subsequently recovering the cations that constitute that product. In terms of selecting the appropriate precursors, for multicomponent products such as PLZT, the mutual solubility of the various ingredients must be considered. The ability to dissolve several precursor salts in a mutual solvent allows for the preparation of homogeneous, multicomponent compositions, which is one of the most significant advantages of chemical coprecipitation. Other advantages include precise control of stoichiometry, the ability to uniformly disperse trace additives, freedom from contamination inherent in powder grinding and mixing operations, and because of the fine particle size of the resulting powders, higher reactivity and therefore lower sintering temperatures.

After preparing a homogeneous solution of the precursors, powder precipitation is accomplished through the addition of at least one complexing ion. For PLZT, frequently OH⁻ in the form of ammonium hydroxide is added as the complexing anion, which results in the formation of an amorphous, insoluble PLZT-hydroxide. Other complexing species that are commonly used are carbonate and oxalate anions. CO₂ gas is used to form carbonates. Irrespective of the complexing anion, the precipitated powders are eventually converted to the desired crystalline oxide phase by low temperature heat treatment.

A key aspect of the coprecipitation process is to ensure that the stoichiometry of the solution is maintained in the precipitated powder through quantitative precipitation of each of the cations in the material. In practice, this is accomplished by simultaneously exceeding the solubility product for each of the cations by adding the correct complexing anion(s) and controlling concentration variables. Theoretically, it is possible to control the precipitate size, size distribution, and morphology through an understanding of precipitation kinetics and control of precipitation variables such as reactor residence time.

Throughout subsequent processing the fine nature of the precipitated powders should be maintained. Minimizing agglomeration during solvent removal and calcination is thus an important aspect of downstream processing. Techniques such as freeze-drying or spray-drying are typically used during solvent removal. Subsequent component fabrication by pressing or other forming operations is similar to that used for powders prepared by the traditional mixed oxide process.

Solution Deposition of Thin Films. Chemical methods of preparation may also be used for the fabrication of ceramic thin films (qv). Metallo-organic precursors, notably metal alkoxides (see ALKOXIDES, METAL) and metal carboxylates, are most frequently used for film preparation by sol-gel or metallo-organic decomposition (MOD) solution deposition processes (see SOL GEL TECHNOLOGY). These methods involve dissolution of the precursors in a mutual solvent; control of solution characteristics such as viscosity and concentration, film deposition by spin-casting or dip-coating, and heat treatment to remove volatile organic species and induce crystallization of the as-deposited amorphous film into the desired structure.

True sol-gel deposition routes have typically utilized solvents such as alcohols, and controlled additions of water to partially hydrolyze the metal alkoxide precursors and thus form polymeric solution species of higher molecular weight. The effects of varying the water to alkoxide molar ratio, and using acid and base catalysts to influence the hydrolysis and condensation reactions that lead to polymer formation are well understood for the silica system, but have been less extensively studied for multicomponent electronic ceramic systems, such as Pb(Zr_{1-x}Ti_x)O₃ and YBa₂Cu₃O_{7-δ}. The effects of chemical modifiers such as chelating agents (qv), on the structures of solution polymeric species and their hydrolysis characteristics have been investigated.

Solution deposition processing has been used to prepare thin films (qv) of PbTiO₃, PZT, PLT, PLZT, BaTiO₃, LiNbO₃, PMN, PMN-PT, PZN-PT, and YBa₂Cu₃O_{7-δ}. For the preparation of PZT thin films, the most frequently used precursors have been lead acetate and zirconium and titanium alkoxides, especially the propoxides. Short-chain alcohols, such as methanol and propanol, have been used most often as solvents, although there have been several successful investigations of the preparation of PZT films from the methoxyethanol solvent system. The use of acetic acid as a solvent and chemical modifier has also been reported. Whereas PZT thin films with excellent ferroelectric properties have been prepared by sol-gel deposition, there has been relatively little effort directed toward understanding solution chemistry effects on thin-film properties.

Alternative Thin-Film Fabrication Approaches. Thin films of electronic ceramic materials have also been prepared by sputtering, electron beam evaporation, laser ablation, chemical beam deposition, and chemical vapor deposition (CVD). In the sputtering process, targets may be metal

(elemental), single-phase oxide, or mixed-phase pressed powder targets. In the preparation of PZT and PLZT thin films, multitarget sputtering using elemental targets or single component oxide targets has been utilized.

Other Applications

Diamond and Refractory Ceramic Semiconductors. Ceramic thin films of diamond, silicon carbide, and other refractory semiconductors (qv), eg, cubic BN and BP and GaN and GaAlN, are of interest because of the special combination of thermal, mechanical, and electronic properties (see REFRACTORIES). The majority of the research effort has focused on SiC and diamond, because these materials have much greater figures of merit for transistor power and frequency performance than Si, GaAs, and InP (13). Compared to typical semiconductors such as Si and GaAs, these materials also offer the possibility of device operation at considerably higher temperatures. For example, operation of a silicon carbide MOSFET at temperatures above 900 K has been demonstrated. These devices have not yet been commercialized, however.

Ferroelectric Thin-Film Devices. Since 1989, the study of ferroelectric thin films has been an area of increasing growth. The compositions studied most extensively are in the PZT PLZT family, although BaTiO₃, KNbO₃, and relaxor ferroelectric materials, such as PMN and PZN, have also been investigated. Solution deposition is the most frequently utilized fabrication process, because of the lower initial capital investment cost, ease of film fabrication, and the excellent dielectric and ferroelectric properties that result.

Numerous uses for PZT PLZT thin films are under investigation. The device that, as of this writing, is closest to commercialization is a nonvolatile memory. This device, which utilizes a ferroelectric thin-film capacitor integrated onto silicon circuitry, provides memory retention when the power is off because of the polarization retention of the ferroelectric capacitor. One and zero memory states arise from the two polarization states, P_R and $-P_R$, of the ferroelectric. Because PZT is radiation-hard, the devices are also of interest for military and space applications.

Decoupling capacitors and dynamic random access memories (DRAMs), are based on the dielectric properties of these materials. Applications based on the electrooptic properties include total internal reflection (TIR) switches, optical interconnects, waveguides, optical image comparators, and optical storage disks (see INFORMATION STORAGE MATERIALS). One of the earliest demonstrations of an optical device was in 1984 (14), when the high speed TIR switching behavior of sputter-deposited PLZT thin films was recognized. Use of these materials as optical storage media has also been investigated. In 1989, photosensitivity and electrooptic coefficients of PZT and PLZT thin films was reported (15). A device configuration suitable for optical information storage was proposed.

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CERAMICS AS ELECTRICAL MATERIALS

For a large number of applications involving ceramic materials, electrical conduction behavior is dominant. In certain oxides, borides (see BORON COMPOUNDS), nitrides (qv), and carbides (qv), metallic or fast ionic conduction may occur, making these materials useful in thick-film pastes, in fuel cell applications (see FUEL CELLS), or as electrodes for use over a wide temperature range. Superconductivity is also found in special ceramic oxides, and these materials are undergoing intensive research. Other classes of ceramic materials may behave as semiconductors (qv). These materials are used in many specialized applications including resistance heating elements and in devices such as rectifiers, photocells, varistors, and thermistors.

Ceramics (qv) are equally important as electrical insulators (see INSULATION, ELECTRIC). For example, glass (qv) and porcelains (see ENAMELS, PORCELAIN OR VITREOUS) are used for both low and high voltage insulation: alumina [1314-28-1], Al₂O₃; beryllium oxide [1304-56-9], BeO; and aluminum nitride [24304-00-5], AlN, ceramics are used as substrates for microelectronics. Ceramics such as silicon nitride [12033-89-5], Si₃N₄, and silicon carbide [12504-67-5], SiC, are strong, less brittle insulators for use in more severe environmental applications (see ADVANCED CERAMICS, ELECTRONIC). For these applications, the ceramic material must also exhibit other important characteristics such as environmental stability, high mechanical strength, and good thermal shock resistance. As substrates for microelectronic packaging applications, a good thermal expansion match with silicon [7440-21-3], Si, in order to reduce thermal stresses, low dielectric constant and loss to enhance signal processing, and high thermal conductivity for heat dissipation are also necessary characteristics. To meet these often conflicting requirements, different substrate formulations, such as those containing Al₂O₃, BeO, mullite [55964-99-3], AlN, Si₃N₄, and SiC, have been developed in which one or more of the desired properties may be emphasized. Ceramic materials are also used as thin-film insulators (see THIN FILMS). Such oxides as silicon dioxide [7631-86-9], SiO₂, AlN, and Al₂O₃ including several type glasses, as well as Si₃N₄, have been developed as thin-film interlayer dielectric insulation for passivation of integrated circuit devices (see INTEGRATED CIRCUITS). Also being developed are diamond insulating films for device applications (see CARBON DIAMOND, SYNTHETIC).

Barium titanate [12047-27-7], BaTiO₃-based compounds, which exhibit high dielectric constants are typically formulated to satisfy specific capacitive and temperature sensing characteristics (see BARIUM COMPOUNDS). These materials are the most widely used electronic materials for disk, multilayer, and thick-film capacitors. However, relaxor-based formulations are also being developed to serve both capacitive and actuator functions. Typically, these consist of lead magnesium niobate (PMN), Pb(MgNb)O₃, modified with Zn, Fe, or Ni as divalent cations and Ti, Nb, Ta, or W as higher valence cations. Important characteristics of these relaxors are their high, frequency-dependent dielectric permittivity, broad dielectric maxima, and low firing temperature, which allow use of less expensive silver palladium electrodes and cofiring in ambient air.

The trend in capacitor technology is increasingly toward integrated device packaging in which the capacitor is embedded in thin- or thick-film form. Development of ferroelectric thin films for nonvolatile memory applications are expected to accelerate this trend (see FERROELECTRICS). Primarily these films are based on lead zirconate-titanate (PZT), Pb(TiZr)O₃, formulations, either vapor deposited or sol-gel derived (see SOL GEL TECHNOLOGY), but other formulations, such as lead titanate (PT), [12060-00-3], PbTiO₃, piezoelectrics lead lanthanum zirconate titanate (PLZT), (PbLa)(TiZr)O₃, and relaxor compositions, are also being developed. These materials in bulk form are all strongly piezoelectric and rapid strides have been made in their development and use as actuator motors, ultrasonic transducers, and for electromechanical sensing. Piezoelectrics (PLZT) also elicit wide interest as electrooptic materials for such applications as high speed shutters, switches, light modulators, and displays.

Besides piezoelectrics, a wide range of ceramic materials have been developed as gas, oxygen, temperature, voltage, and humidity sensors. Typically, these are based on semiconducting oxides such as titanium dioxide [13463-67-7], TiO₂, zinc oxide [1314-13-2], ZnO, modified BaTiO₃, tin dioxide [18282-10-5], SnO₂, and chromium magnesium oxide [12053-26-8], MgCr₂O₄. Because many of these sensors can provide a feedback signal for process control, ie, serve as smart sensors, these materials represent an expanding area of ceramic exploration and development. For oxygen sensing, solid electrolyte conductors such as yttria [1314-36-9], Y₂O₃, stabilized ZrO₂ are the most widely used, particularly for automotive applications, but TiO₂ is also being developed as an oxygen sensitive resistive sensor.

Ferrites (qv) are ceramic oxide materials that exhibit ferrimagnetic properties, by virtue of the opposed (A-B coupling) and variable cation orientation within the material. Developments in ferrites have been related primarily to use in recording heads, but research in the area of microwave ferrites is also active (see INFORMATION STORAGE MATERIALS; MICROWAVE TECHNOLOGY). Categories of ferrite include hard, soft, and microwave materials. All are based primarily on ferric oxide [1309-37-1], Fe₂O₃. The hard ferrites are of composition MeO·6Fe₂O₃, where Me = Sr, Ba, etc. This class of materials is used in permanent magnets and for motor applications. Soft ferrites, MeO·Fe₂O₃, are based on the cubic spinel structure, Me = Ni, Co, Cu, Zn, Mn, and are readily switchable and modified. These are used in computer memory cores, deflection yokes, telecommunication switching, and other applications. Microwave ferrites are based on the garnet structure and also contain iron oxide, eg, 3Y₂O₃·5Fe₂O₃. They feature high resistivity and high frequency capability.

Developments in high temperature ceramic superconductors have targeted a number of important potential applications for these materials including thin-film devices, microwave applications, energy storage, and in microelectronics. The structure of the ceramic superconductors is based mainly on an oxygen deficient, layered perovskite structure. Formulations in the Y-Ba-Cu-O system (YBa₂Cu₃O_{7-x}) have been most successfully developed. Processing aspects of superconductors in order to achieve useful shapes, controlled microstructures, and high current density materials are significant challenges.

In the broad range of ceramic materials that are used for electrical and electronic applications, each category of material exhibits unique property characteristics which directly reflect composition, processing, and microstructure. Detailed treatment is given primarily to those property characteristics relating to insulation behavior and electrical conduction processes. Further details concerning the more specialized electrical behavior in ceramic materials, eg, polarization, dielectric, ferroelectric, piezoelectric, electrooptic, and magnetic phenomena, are covered in References 1–9.

Electrical Conduction Phenomena

Materials are usually classified according to the specific conductivity mode, eg, as insulators, which have low conductivity and low mobility of carriers. Metallic conductors, which include some oxides, have a high conductivity value which is not a strong (exponential) function of temperature. Semiconductors are intermediate and have an exponential temperature dependence. Figure 1 gives examples of electrical conductivities at room temperature for these various materials.

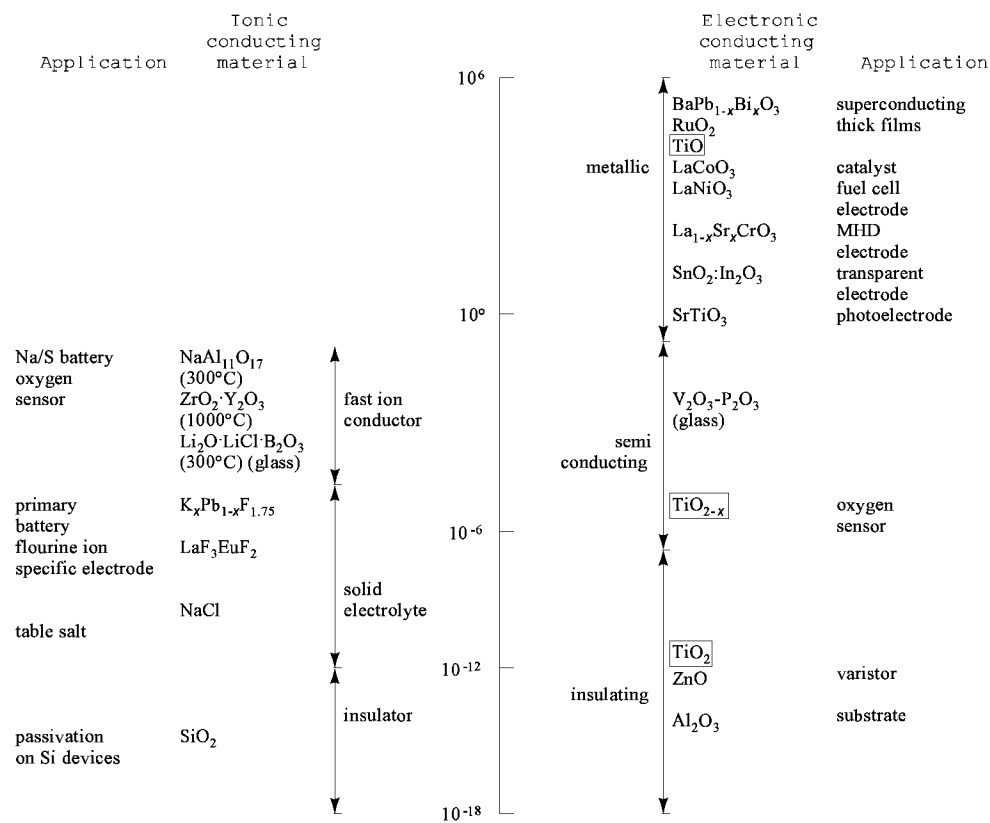


Fig. 1. Logarithmic scale of the electrical conductivities of materials categorized by magnitude and carrier type, ie, ionic and electronic, conductors. The various categories and applications are given. The wide conductivity range for the different valence defect states of Ti oxide is highlighted. MHD is magnetic hydrodynamics.

The electrical characteristics of ceramic materials vary greatly, since the atomic processes are different for the various conduction modes. The transport of current may be because of the motion of electrons, electron holes, or ions. Electrical ceramics are commonly used in special situations where refractoriness or chemical resistance are needed, or where other environmental effects are severe (see REFRATORIES). Thus it is also important to understand the effects of temperature, chemical additives, gas-phase equilibration, and interfacial reactions.

Consider a ceramic solid at equilibrium with its environment in terms of temperature, pressure, and composition, and then apply an electric field, $E = -dV/dx$, defined as V/m. The ions and electrons reestablish equilibrium by moving in the field which results in a net electric current density j defined as C/(m²s) or A/m². An electron or an electron hole has a unit charge, $e = 1.601 \times 10^{-19}$ C; an ion has this unit charge times its valence (z) ze . Thus the current density owing to the flow of particles of species i is given by:

$$j_i = n_i z_i e v_i \tag{1}$$

where n_i is the number of i particles per cubic meter and v_i is the average drift velocity or net velocity in the direction of the applied field.

A general observation, verified for nearly all solids, is a proportionality between current density and field strength, known as Ohm's law. The electrical conductivity ς is this proportionality constant and is defined as

$$\sigma = j/E \quad 1/(\Omega\text{m}) \tag{2}$$

Thus when an electric field is applied to a solid material the mobile charge carriers are accelerated to an average drift velocity v , which, under steady-state conditions, is proportional to the field strength. The proportionality factor is defined as the mobility, $\mu = v/E$. An absolute mobility B_i , defined as the velocity per unit driving force acting on the particle, is given as:

$$B_i = v_i/\text{force} = v_i/z_i e E \tag{3}$$

Hence, the conductivity ς_i associated with the drift of the particles is given as:

$$\sigma_i = n_i z_i e (v_i/E) = n_i z_i^2 e^2 B_i \tag{4}$$

The conductivity becomes complex if more than one type of charge carrier is present and involved in the conduction process. The total conductivity is the sum of all the conduction associated with the net motion of electrons, holes, and ions, ie:

$$\sigma = \sigma_1 + \sigma_2 + \sigma_3 + \cdots \sigma_n = \sum \sigma_i \quad (i = 1 \cdots n) \tag{5}$$

The fraction of the total conductivity at a specific temperature and composition owing to the conduction of specie i is called the transference number

$$t_i = \sigma_i/\sigma \tag{6}$$

where the value of t lies between 0 and 1.0. The transference numbers for the charged species in several compounds are given in Table 1 where t^+ and t^- represent the transference number for cation and anion transport respectively, and $t_{e,h}$ that for electronic transport via electrons or holes. The cerium(IV) oxide [1306-38-3]-zirconium oxide [1314-23-4], CeO₂-ZrO₂, system is an example of variable transference number in an ionic system. Figure 2 illustrates the range of ionic transference numbers for this material as it varies from 0.03 to 1.0, depending on temperature and composition.

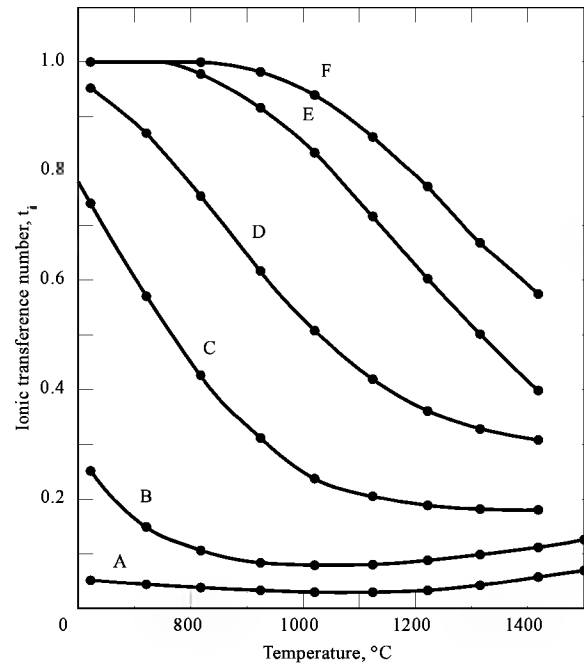


Fig. 2. Ionic transference number of CeO₂-ZrO₂ compositions versus temperature. Concentrations of CeO₂ in mol % are A, 80; B, 50; C, 40; D, 33; E, 25; and F, 18 (10).

Table 1. Transference Number of Cations t^+ , Anions t^- , and Electrons or Holes $t_{e,h}$ in Several Compounds^a

Compound	Temperature, °C	t^+	t^-	$t_{e,h}$
AgCl	20–350°C	1.0		
CuCl	20°C	0.0		
	366°C	1.0		
KCl	435°C	0.96	0.04	
	600°C	0.88	0.12	
KCl + 0.02% CaCl ₂	430°C	0.99	0.01	
	600°C	0.99	0.01	
NaCl	400°C	1.0		
	600°C	0.95	0.05	
Na ₂ O·11Al ₂ O ₃	<800°C	1.0 ^b		<10 ⁻⁶
Na ₂ O·CaO·SiO ₂		1.0 ^b		
BaF ₂	500		1.0	
ZrO ₂ + 7% CaO	>700°C		1.0	10 ⁻⁴
ZrO ₂ + 18% CeO ₂		1500°C	0.52	0.48
ZrO ₂ + 50% CeO ₂	1500°C		0.15	0.85
FeO	800°C	10–4	0.0	1.0

^a Ref. 1.
^b Value is for sodium ion.

The electrical conductivity is one of the few physical quantities that has been found to vary by many orders of magnitude, ranging from 10⁵ (Ωcm)⁻¹ for conducting oxides such as rhenium(VI) oxide [1314-28-9], ReO₃, or chromium(IV) oxide [12018-01-8], CrO₂, to 10⁻¹⁴ (Ωcm)⁻¹ for highly insulating materials such as steatite porcelain. Certain compounds exhibit changes in conductivity by several orders of magnitude as a result of doping, temperature, or processing effects.

Ionic Conduction Phenomena

For an ion to move through the lattice, there must be an empty equivalent vacancy or interstitial site available, and it must possess sufficient energy to overcome the potential barrier between the two sites. Ionic conductivity, or the transport of charge by mobile ions, is a diffusion and activated process. From Fick's Law, $J = -D(dn/dx)$, for diffusion of a species in a concentration gradient, the diffusion coefficient D is given by

$$D = \alpha \lambda^2 \nu = \alpha \lambda^2 \nu_0 e^{-\Delta G^+ / kT}$$
 (7)

where λ is the jump distance and is approximately equal to a lattice parameter ($a \sim 3 \times 10^{-8}$ cm) or an adjacent plane, α is the number of possible jump sites, and ν is the jump frequency, ν_0 is approximately 10¹³ s⁻¹, the natural vibrational frequency, and ΔG^+ is the free energy of activation. The diffusion coefficient of the ion D_i is related to the Einstein relation by the mobility

$$D_i = \mu_i kT / e z_i = B_i kT$$
 (8)

The equations generally developed include all forms of the conduction. For example, to determine the flux or conductivity of ions in a solid electrolyte as compared to electrons in a semiconducting ceramic, two terms are of interest: the number of charge carriers and the mobility. The effects of temperature, composition, and structure on each of these terms must also be considered.

Ions in ceramic crystalline materials constitute potential charge carriers that can contribute to electrical conductivity, but analysis requires a

determination of the concentration and mobility of the charge carriers. As indicated, for an ion to move through the lattice under the driving force of an electric field it must gain sufficient thermal energy to surmount the free energy barrier, ΔG^* , at the intermediate position between the lattice sites. The result is a mobility that depends on the ion jumping from site to site. For example, by comparison with equations 4 and 5, the ion mobility for a rock salt-crystal structure when $\alpha = 6$ is expressed as

$$\mu_i = \frac{(6 e z_i a^2 \nu)}{kT} e^{-\Delta G^* / kT}$$

(9)

The absolute mobility is given in equation 10, which is again the Einstein relationship.

$$B_i = (6 a^2 \nu) / kT e^{-\Delta G^* / kT} = D_i / kT$$

(10)

Equation 11 gives the conductivity for a particular ion having a transference number, t_p in a crystal, which is the Nernst-Einstein relationship.

$$\sigma_i = t_i \sigma = (D_i n_i z_i^2 e^2) / kT$$

(11)

These equations represent expressions for the extrinsic ionic conductivity of the material as exhibited by the shortened defect notation of equation 12, showing that Na vacancies are created by doping and not primarily generated from thermal energy.



In pure and stoichiometric compounds, intrinsic defects are formed for energetic reasons. Intrinsic ionic conduction, or creation of thermal vacancies by Frenkel, ie, vacancy plus interstitial lattice defects, or by Schottky, cation and anion vacancies, mechanisms can be expressed in terms of an equilibrium constant and, therefore, as a free energy for the formation of defects, ΔG_f . If the ion is to jump into a normally occupied lattice site, a term for the creation of vacancies must be included. This results in an added exponential term in the conductivity expression in equation 11, and is valid when the concentration of defects caused by impurities is less than that caused by thermal energy (eq. 13).

$$\sigma_i = \frac{n_i z_i^2 e^2}{kT} e^{-\Delta G^* / kT} e^{-\Delta G_f / kT}$$

(13)

The term $e^{-\Delta G_f / kT}$ is the probability that a site is vacant. Diffusion coefficients as a function of temperature for representative ceramic materials are given in Figure 3.

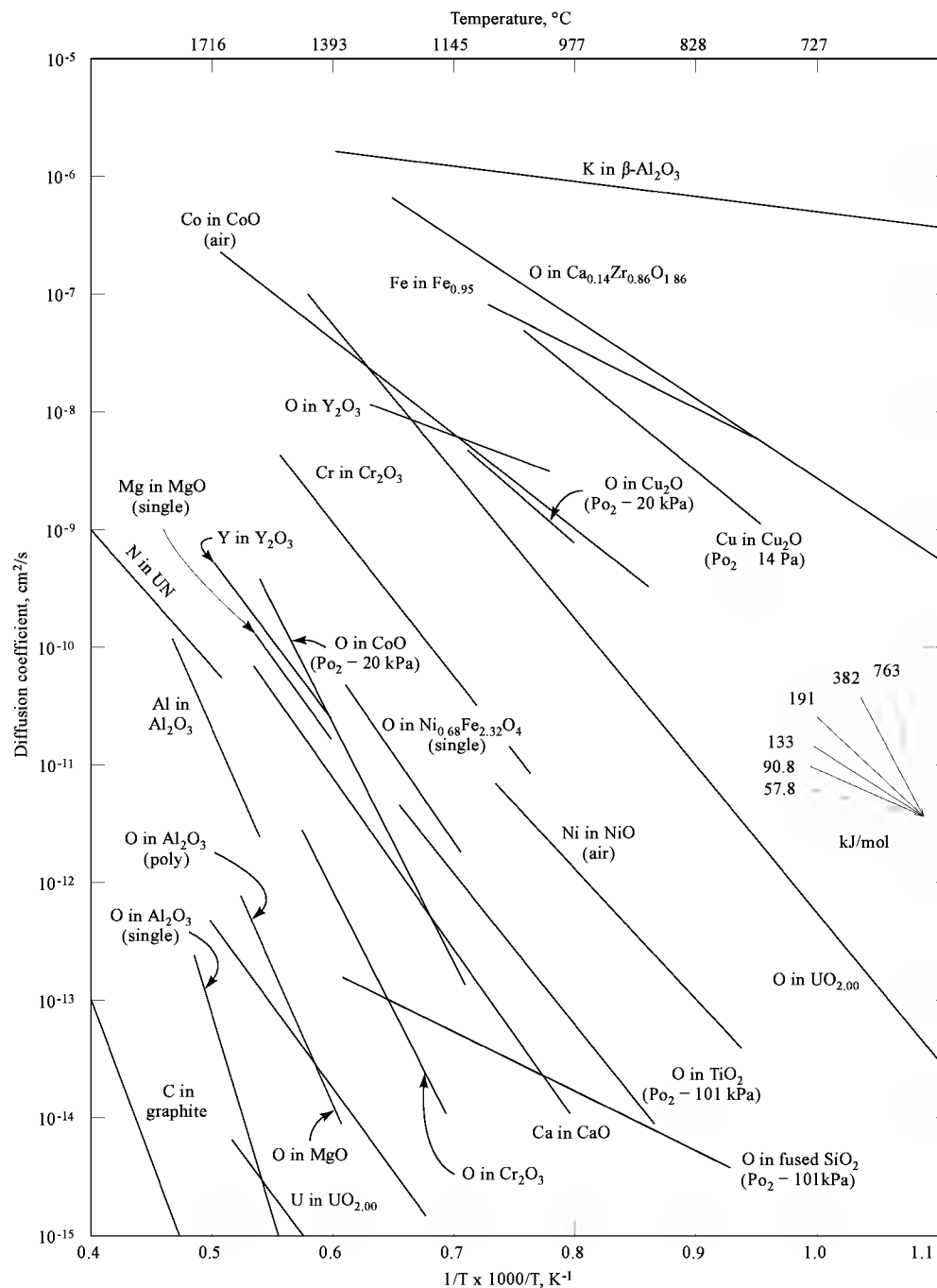


Fig. 3. The diffusion coefficients of several single-crystal and polycrystalline ceramic materials as a function of temperature where P_{O_2} represents the partial pressure of oxygen. The activation energy is obtained from the slope and the insert; eg, for O diffusion in $Ca_{0.14}Zr_{0.86}O_{1.86}$, ie, $ZrO_2 + 14$ cation % Ca, $\Delta G^+ \sim 121$ kJ mol. To convert kJ to kcal, divide by 4.184; to convert kPa to psi, multiply by 0.145.

In nonstoichiometric and doped materials the defect structure is generally more complex. In this extrinsic region the defect concentration is nearly temperature independent and depends primarily on the number and valence state of the solute atoms. For many materials, temperature ranges can be found in which only one type of charge carrier, intrinsic or extrinsic, is dominant. These regions can be distinguished by different activation energies as illustrated in Figure 4, where intrinsic conduction is dominant at elevated temperatures (11).

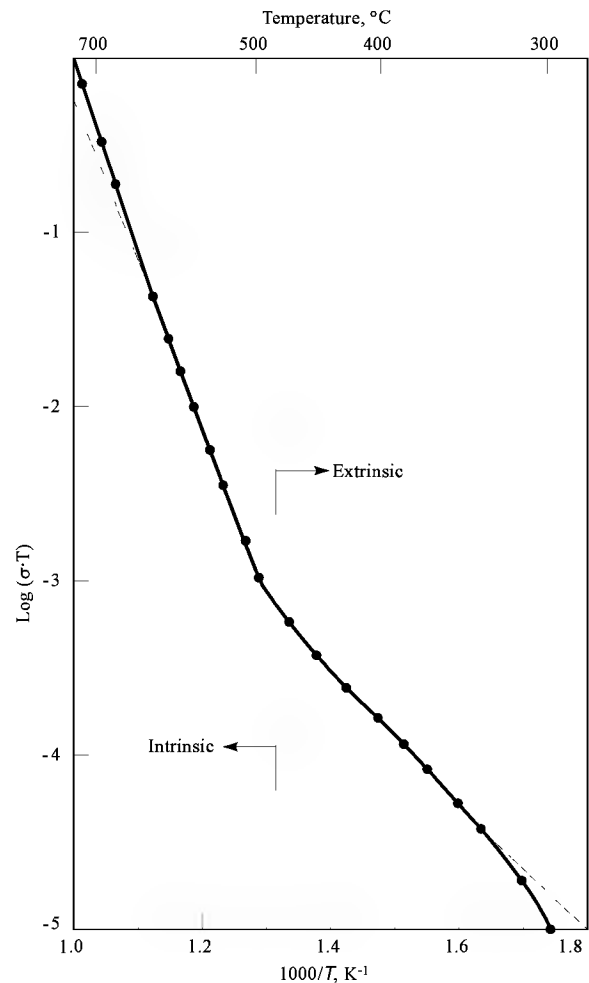
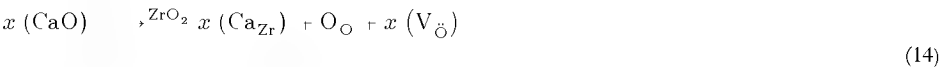


Fig. 4. Modified Arrhenius diagram of the ionic conductivity of sodium chloride. T is in Kelvin, σ is in $(\Omega\text{cm})^{-1}$. Over the temperature range shown the sodium ions are the primary charge carriers (11).

When aliovalent, ie, different valence, impurities are added to an ionic solid, the crystal lattice compensates by forming defects that maintain both electrical neutrality and the anion to cation ratio of the host lattice. For example, addition of x mol of CaO to ZrO_2 requires the formation of x mol of oxygen vacancies.



If this concentration is larger than the oxygen vacancies created by thermal effects, then the conductivity from the motion of the doubly charged ions is directly proportional to the concentration of CaO (eq. 15).

$$\sigma_{\text{O}^{2-}} = \frac{([\text{CaO}](2)^2 e^2)}{kT} e^{-\Delta G^+ / kT} \tag{15}$$

In polycrystalline materials, ion transport within the grain boundary must also be considered. For oxides with close-packed oxygens, the O-ion almost always diffuses much faster in the boundary region than in the bulk. In general, second phases at grain boundaries are less close packed and provide a pathway for more rapid diffusion of ionic species. Thus the simplified picture of bulk ionic conduction is made more complex by these additional effects.

Fast Ion Conductors

Several types of compounds showing exceptionally high ionic conductivity have become of technological interest: (1) halides and chalcogenides of silver and copper in which the metal atom is disordered over a large number of interstitial sites; (2) oxides having the β -alumina [12005-48-0], $\text{NaAl}_{11}\text{O}_{17}$, structure in which conduction channels are formed for the monovalent cation, resulting in high mobilities; and (3) oxides of the fluorite [14542-23-5], CaF_2 , structure in which large concentrations of defects are caused either by a variable-valence cation or by solid solution from a second cation of lower valence; eg, CaO-ZrO_2 or $\text{Y}_2\text{O}_3\text{-ZrO}_2$. Figure 5 shows electrical conductivity data for some representative high conductivity materials. The values are many orders of magnitude larger than for normal ionic compounds and are comparable to the conductivity of such liquid electrolytes as dilute solutions of sulfuric acid.

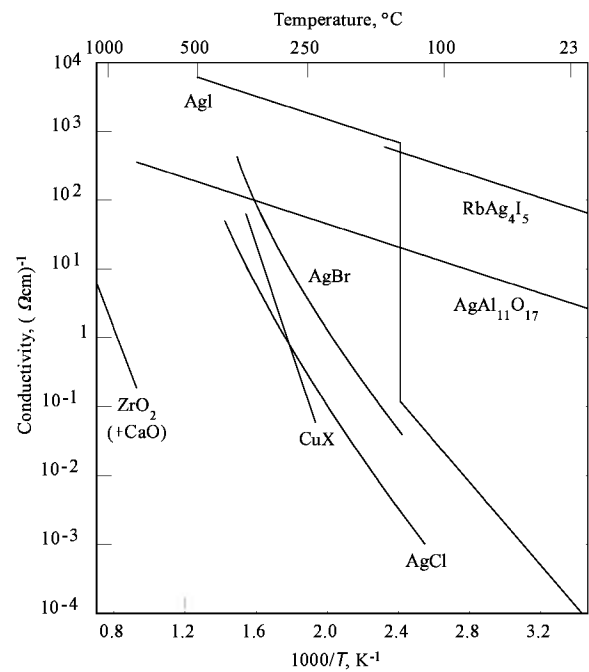


Fig. 5. Conductivity as a function of temperature for some highly conducting solid electrolytes, where X in CuX is Cl, Br, or I (11).

Particular interest has been shown in stable materials having high ionic conductivities ($t_i \approx 1$) because of applications as solid electrolytes (Table 2). Owing to the precise relationship between the voltage and the chemical potential gradient across the electrolyte, these materials can be used in batteries (qv), fuel cells (qv), and as ion pumps or ion-activity probes. For example, the β -alumina fast ion conductors are used as electrolytes for the sodium–sulfur storage battery. The β -aluminas are hexagonal in structure having approximate composition $AM_{11}O_{17}$, where A, the mobile conducting ion, is monovalent Na, and the M ion is trivalent Al. The crystal structure consists of four planes of oxygens in a cubic close-packed sequence, comprising a slab wherein aluminum ions occupy octahedral and tetrahedral sites as in spinel [1302-67-6], Al_2MgO_4 . These spinel blocks are bonded together by a more open layer consisting of the monovalent ions and oxygen. This loosely bound layer is somewhat disordered and provides a two-dimensional path for rapid migration of the monovalent ions by greater than single jump distances.

Table 2. Fast Ion Conductors

Compound	Temperature, °C	Conducting ion	$\sigma_{ion}, (\Omega m)^{-1}$
$NaAl_{11}O_{17}$	300°C	Na	35
$Na_3OZr_2PSi_2O_{12}$	300°C	Na	20
$CeO_2 + 12 \text{ mol } \% \text{ CaO}$	700°C	O	4
$ZrO_2 + 12 \text{ mol } \% \text{ CaO}$	1000°C	O	0.8
$K_{14}Fe_{11}O_{17}$	300°C	K	2
$Li_2B_4O_7^a$	150°C	Li	10^{-4}
	400°C	Li	0.1
$Li_4B_7O_{12}Cl^a$	300°C	Li	0.2
crystal	300°C	Li	0.8

^a Glass.

In the sodium–sulfur storage battery above 300°C, the overall chemical reaction occurs between molten sodium metal and sulfur to form sodium polysulfide. The cell voltage is related to the activity of the sodium (a_{Na}) in the sulfide relative to its activity in the metal.

$$V = \frac{RT}{F} \ln [a_{Na}(\text{sulfide}) / a_{Na}(\text{metal})]$$

(16)

Using excess voltage, ions can be pumped from the low concentration (activity) side of the electrolyte to the high activity side, during which the storage battery is charged. In another application, the ion activity on one side can be fixed at a known value and the activity on the other side determined for various unknown conditions.

Other important fast ion conductors are the oxides having a fluorite structure, eg, ZrO_2 . High (10–20 mol %) dopant levels of calcium oxide [1305-78-8] CaO , or Y_2O_3 in solid solution with the ZrO_2 lead to large defect concentrations and vacancy ordering. The concentration of the vacancies is produced during processing. For example, for each Ca^{2+} that substitutes for a Zr^{4+} ion, an oxygen vacancy must result, so that charge balance is maintained (eq. 14). Rapid oxygen migration occurs in these materials because of the high (15%) concentration of vacancies and correlated ion jumps over distances greater than the interionic separation. This high ionic conduction results from the combination of the high oxygen vacancy concentration and high anion mobility (12). These structures support high oxygen ion mobility as a result of the low fourfold coordination of cations around the oxygens, coupled with the interconnected nature of the face-shared polyhedra that surround the oxygen sites (12).

The doped ZrO_2 structures are used as electrochemical sensors, as, for example, when used to detect oxygen in automotive exhaust (see EXHAUST CONTROL, AUTOMOTIVE). The sensor voltage is governed by the Nernst equation (eq. 17) where the activities are replaced by oxygen partial pressures and the air inside the chamber ($P_{O_2}^{II}$) is used as reference.

$$E = \frac{RT}{4F} \ln \left(\frac{P_{O_2}^I}{P_{O_2}^{II}} \right)$$

(17)

where E is the voltage across the material, F is the Faraday constant (96,487 C), and R is the gas constant (8.314 V C / K). A porous platinum electrode is used so that the oxygen can pass through the electrode and react with the gas sensor material. Oxygen ions move

freely through the $\text{ZrO}_2\text{--Y}_2\text{O}_3$ crystal and develop a potential difference as a result of the differential oxygen partial pressure (12,13).

Glass Conduction

Electrical conduction in glasses is mainly attributed to the migration of mobile ions such as Li^+ , Na^+ , K^+ , and OH^- under the influence of an applied field. At higher temperatures, $>250^\circ\text{C}$, divalent ions, eg, Ca^{2+} and Mg^{2+} , contribute to conduction, although their mobility is much less (14). Conduction in glass is an activated process and thus the number of conducting ions increases with both temperature and field. The temperature–resistivity dependence is given as:

$$\rho = \frac{1}{[6kT \lambda \nu \alpha (ez) n] e^{E/kT}}$$

(18)

where ν is the natural vibration frequency (10^{13} s^{-1}); λ is the average jump distance ($\sim 0.8\text{--}0.9 \text{ nm}$; α is the number of adjacent sites (~ 3); n is the concentration of charge carriers; and E is the activation energy.

As the concentration n of modifier ion increases, the effect is to loosen the structure, resulting in freer migration of the conducting ions and a lowering of the activation energy E . The jump distance and the number of adjacent sites greatly affect the mobility of the ions when two or more mobile species are present. Conductivity may decrease through a blocking effect or mutual reduction in the mobilities, described as the mixed alkali effect (14).

Fast ion conduction may occur in certain glasses such as silver and alkali borates, phosphates, and molybdates (15). The criteria for such conduction is the existence of a highly ordered structure having channels in which ions can easily move within the sublattice. Because fast ion conduction occurs in glasses that are amorphous solids, the mechanisms must be attributed to other structural factors (12). Glasses have a random network and only short-range order, typically a few atom spacings. Even though the glass structure can be described as open, because of its random nature, there is no well-defined channel for conduction as found in ceramic materials. The creation of structural disorder occurs during fusion of the glass and, as in lithium borate glass, is presumed to result from the formation of a large excess of nearly equivalent sites, giving enhanced ionic mobility and conductivity (15).

Electronic Conduction in Ceramics

The relatively high mobilities of conducting electrons and electron holes contribute appreciably to electrical conductivity. In some cases, metallic levels of conductivity result; in others, the electronic contribution is extremely small. In all cases the electrical conductivity can be interpreted in terms of carrier concentration and carrier mobilities. Including all modes of conduction, the electronic and ionic conductivity is given by the general equation:

$$\sigma_t = \sigma(t_{\text{ionic}} + t_{\text{electronic}})$$

(19)

where the total electronic conductivity is given as:

$$\sigma = ne\mu_n + pe\mu_p$$

(20)

n and p denote the concentrations of electrons and holes, respectively, and μ_n and μ_p are the corresponding mobilities. The mobility of these electronic defects are generally much higher than those of ionic defects because they are of lower mass and charge density and less confined to particular atomic sites (1,11). Scattering of electrons and holes occurs by phonons, point defects, dislocations, and grain boundaries. The conductivity is also determined by the concentration of electrons and holes, and is generally described by energy band structures (11). Figure 6 schematically illustrates the three band energy configurations corresponding to intrinsic metal, semiconductor, and insulator conduction. The highest energy band, which is completely filled at $T = 0 \text{ K}$, is called the valence band, whereas the next higher band, being empty at this temperature, is the conduction band. These energy levels are separated by an energy or band gap (E_g), which normally is not occupied by electrons (11). The band gaps of several materials are given in Table 3. As shown by Figure 6, at $T > 0 \text{ K}$, metallic conduction occurs in ceramic materials where there are partially filled valence bands and a corresponding overlap with the unoccupied conduction band states. When a small energy band gap is present with no overlap, semiconduction results. If a large energy gap occurs the materials are insulating, because the energy gap is too great to thermally promote electrons into the conduction band. Thus, with sufficient energy input, conduction occurs either by electrons being promoted into the conduction band or through the electron holes left behind in the valence band. If a semiconductor or insulator contains defects, ie, dopants, impurities, or vacancies, which have states within the band gap, as donor or acceptor levels, the result is an increase in conduction (1).

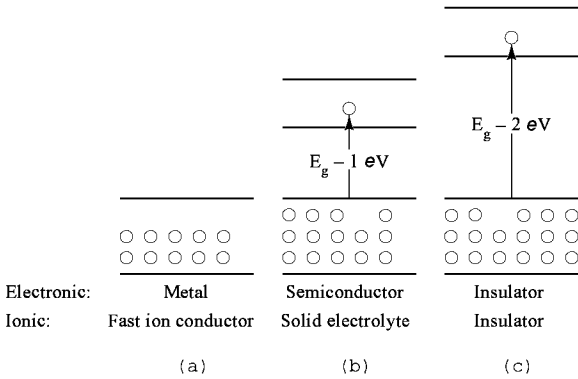


Fig. 6. Schematic of band gap energy, E_g , for the three types of electronic and ionic conductors. For electronic conductors the comparison is made of the relative occupancy of valence and conduction bands. For ionic conductors, the bands correspond to the relative occupancy of ionic sublattices. For (a), $n = 10^{22} \text{ mL}^{-1}$ for (b), $n = 10^{10} \text{ mL}^{-1}$; and for (c), $n = 1 \text{ mL}^{-1}$. (12).

Table 3. Energy Gap (E_g) at Room Temperature for Intrinsic Semiconductors

Crystal	$E_g, \text{ eV}$	Crystal	$E_g, \text{ eV}$
Cu_2O	2.1	Si	1.1
BaTiO_3	3.0–3.2	$\alpha\text{-SiC}$	2.8–3.0
ZrO_2	3.2	BN	4.8
Fe_2O_3	3.4	C, diamond	5.2–5.6
ZnO	3.5		

TiO ₂	3.05–3.8	AgI	2.8
CoO	4	KCl	7
BaO	5.5	CaF ₂	12
CeO ₂	5.5		
BeO	7.1	PbS	0.35
MgO	>7.8	GaAs	1.4
Al ₂ O ₃	>8	GaP	2.25
SiO ₂	~9	ZnS	3.6

Ordinarily, the energy gap (E_g) between the filled and empty bands is appreciably greater than *kT*. The concentration of conduction electrons *n* in the pure stoichiometric material is equal to the concentration of holes *p* and is given by

$$n = p = 2 \left(\frac{2 \pi k T}{h^2} \right)^{3/2} (m_e^* m_h^*)^{3/4} e^{-(E_g / 2kT)}$$

(21)

Where *h* is Planck's constant and *m_e^{*}* and *m_h^{*}* are the effective masses of the electron and hole which may be larger or smaller than the rest mass of the electron. The effective mass reflects the strength of the interaction between the electron or hole and the periodic lattice and potentials within the crystal structure. In an ideal covalent semiconductor, electrons in the conduction band and holes in the valence band may be considered as quasi-free particles. The carriers have high drift mobilities in the range of 10 to 10⁴ cm² (Vs) at room temperature. As shown in Table 4, this is the case for both metallic oxides and covalent semiconductors at room temperature.

Table 4. Carrier Mobilities at Room Temperature

Mobility, cm ² (Vs)			Mobility, cm ² (Vs)		
Crystal	Electrons	Holes	Crystal	Electrons	Holes
Si	1500	450	CoFe ₂ O ₄	10 ⁻⁴	10 ⁻⁸
diamond	1800	1200	CoO		~0.1
			NiO		~0.1
			Fe ₃ O ₄		0.1
AgCl	50		Fe ₂ O ₃	0.1	
KBr	100		TiO ₂	0.2	
			(BaLa)TiO ₃	0.5	0.1
AlN		10	BaO	5	
GaP	150	120	SrTiO ₃	6	
PbS	600	200	ZnO	50	
GaAs	8500	450	SnO ₂	160	

Two types of scattering affect the motion of electrons and holes. Lattice or phonon scattering, resulting from thermal vibrations of the lattice, gives increasing amplitude of vibration with temperature. The associated mobility decreases according to the relationship: $\mu_i \sim T^{-3/2}$. A second source of scattering arises from the presence of impurities at low (<100 K) temperature, which distort the periodicity of the lattice, giving a mobility relationship $\mu_i \sim T^{-1/2}$. The total mobility μ is proportional to the sum of these two terms. The temperature dependence of the mobility term for quasi-free electrons and holes is much smaller than that for their concentration which is exponential. As a result, the conductivity has a temperature dependence chiefly determined by the concentration term.

In ionic host lattices, where there is interaction between neighboring ions, a polarization of the lattice associated with the presence of electronic carriers can occur. The resulting charged entity, consisting of the electronic carrier plus its polarization field, is referred to as a polaron. When the association is weak (large polaron), conductivity similar to quasi-free electrons results having a small effective mass. When the linear dimension of the electronic carrier plus the lattice distortion is smaller than the lattice parameter (small polaron), the mobility is strongly affected by the lattice distortion which must move along with the electronic carrier. This process is loosely referred to as a "hopping" mechanism. This is a simplification of the mechanism because discrete energy levels become localized states of lower energies within the band gap (16). Polar motion then becomes possible as a result of small overlap of the wave functions of neighboring positions. Conduction results in a change in the local polarization field and local lowering of the energy state. Electron mobility increases according to the degree of overlap of the partially filled local state and not through conduction bands (16). Mobility of the small polarons is typically less than 1 cm² (Vs) but can be much lower.

Electronic Conducting Ceramics

High Electronic Conductivity. Metals are not the only materials that exhibit metallic conductivity. Some transition-metal oxides also have high levels of conductivity resulting from overlap of the electron orbitals forming wide, unfilled *d* or *f* electron energy bands having concentrations of quasi-free electrons of 10²²–10²³ mL⁻¹. This is equivalent to metallic conduction. The perovskite and rutile oxide structures have been the most studied. The electronic conductivity can be very high and show little temperature dependence, ie, be of the metallic type. The mobility of the electrons is usually less than 1 cm² (Vs). The range of electronic conductivities in simple transition-metal oxides is broad (10⁻⁴–10⁴ (Ωcm)⁻¹) and the temperature dependencies vary dramatically.

Metallic conduction occurs in transition-metal oxides such as ReO₃, CrO₂, vanadium(II) oxide [12035-98-2], VO, titanium(II) oxide [12137-20-1], TiO, and rhenium(IV) oxide [12036-09-8], ReO₂; in doped perovskite structures such as lanthanum titanium oxide [12201-04-6], LaTiO₃, calcium vanadium(IV) oxide [12138-49-7], CaVO₃, BaTiO₃, strontium ferrate (1:1) [12022-69-4], SrFeO₃, lanthanum nickelite [12031-18-4], LaNiO₃, lanthanum cobaltite [12016-86-3], LaCoO₃, and lanthanum chromite [12017-94-6], LaCrO₃; in many of the tungsten bronzes, Na_xWO₃, La_xWO₃ and Na_xNb₂O₅, and in some spinels, Li_{0.5}In_{0.5}Cr₂S₄, typically at specific dopant concentrations. These materials are technologically significant as potential fuel cell electrodes. In microelectronics, ReO₂ and RuO₂ ruthenium(IV) oxide [12036-10-1] compounds are used in organic and inorganic pastes as the conducting component and are applied as thick films followed by a firing step.

Semiconducting Ceramics. Most oxide semiconductors are either doped to create extrinsic defects or annealed under conditions in which they become nonstoichiometric. Although the resulting defects have been carefully studied in many oxides, the precise nature of the conduction is not well understood. Mobility values associated with the various charge transport mechanisms are often low and difficult to measure. In consequence, reported conductivities are often at variance because the effects of variable impurities and past thermal history may overwhelm the dopant effects.

A list of some impurity semiconductors is given in Table 5. Because impurity atoms introduce new localized energy levels for electrons that are intermediate between the valence and conduction bands, impurities strongly influence the properties of semiconductors. If the new energy levels are unoccupied and lie close to the top of the valence band, electrons are easily excited out of the filled band into the new acceptor levels, leaving electron holes

in the valence band that contribute to electrical conductivity. These *p*-type oxide conductors commonly represent nonstoichiometric compositions with decreased metal content and are sometimes called deficient semiconductors. If the impurity additions have filled electron energy levels close to the conduction band, electrons may be excited from these donor levels into the conduction band where they contribute to the conductivity. This type of conductor commonly results from nonstoichiometric compositions having excess metal content, the so-called excess metal semiconductors.

Table 5. Impurity Semiconductors

<i>n-Type</i>					
Cds	BaTiO ₃	Nb ₂ O ₅	Fe ₂ O ₃	WO ₃	GeO ₂
CdSe	SrTiO ₃	Ta ₂ O ₅	Tl ₂ O ₃	TiO ₂	MnO ₂
ZnF ₂	PbCrO ₄	Fe ₃ O ₄	In ₂ O ₃	SnO ₂	ZnO
<i>p-Type</i>					
Se	CuI	Ag ₂ O	Hg ₂ O	NiO	PdO
Te	SnS	Cu ₂ O	MnO	FeO	CoO
<i>Amphoteric</i>					
Si	Sn	PbSe	Ti ₂ S	Al ₂ O ₃	Mn ₃ O ₄
Ge	PbS	SiC	PbTe	Co ₃ O ₄	UO ₃

Silicon carbide can be doped using boron [7440-42-8] to provide acceptor levels within the band gap (0.3 eV above the valence band), thus making it a *p*-type conductor, or nitrogen can be added to provide donor levels and *n*-type conduction (0.07 eV) below the conduction band.

Strontium titanate [12060-59-2], SrTiO₃, becomes an *n*-type semiconductor when additional electrons are created on the Ti lattice sites by donor doping or when oxygen is removed from the material through heat treatment in a reducing atmosphere. The mobility of the electrons in the conduction band is about 6 cm² (Vs). On the other hand, when ZnO is reduced, zinc interstitials are formed and these act as donors, each yielding a free electron.

Copper(I) oxide [1317-39-1] is a *p*-type semiconductor, Cu₂_xO, in which proper vacancies act as acceptors to create electron holes that conduct within a narrow band in the Cu *d*-orbitals. Nickel monoxide [1313-99-1], NiO, forms a deficient semiconductor in which vacancies occur in cation sites similar to those for cuprous oxide. For each cation vacancy two electron holes must be formed, the latter assumed to be associated with regular cations ([Ni²⁺ ·] = Ni³⁺). Semiconduction results from the transfer of positive charges from cation to cation through the lattice. Conduction of this type is similar to the polaron conduction described, where localized sites become polarized, except that the conduction is by electron hole motion. This charge-transfer process corresponds to a low mobility [0.1 cm² (Vs)].

Pure and almost stoichiometric NiO shows, therefore, a very low conductivity of about 10⁻¹³ (Ωcm)⁻¹ at 25°C but, as illustrated in Figure 7, this value can be increased to about 1 (Ωcm)⁻¹ by the addition of lithium (11). This stabilizes the formation of the Ni³⁺ states at a higher concentration, resulting in higher and more reproducible conductivities. Similarly, the insulating characteristics of NiO can be improved by the addition of a stable trivalent ion such as Cr³⁺ in solid solution. This addition decreases the fraction of Ni³⁺ ions formed. Because electron transfer between Ni²⁺ and Cr³⁺ is not favorable, the overall conductivity is substantially decreased.

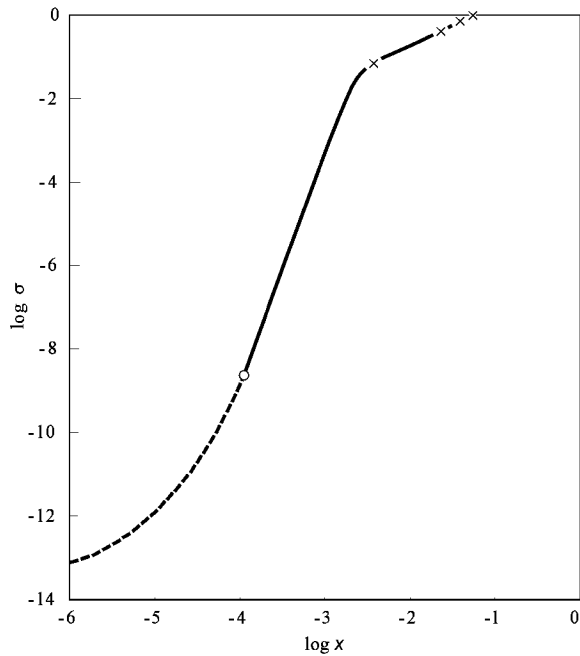


Fig. 7. Electrical conductivity at 23°C of Li-doped NiO, Li_xNi_{1-x}O. σ is in units of (Ωcm)⁻¹ (11).

Similar results can be obtained in many other systems of both *n*- and *p*-type semiconductors. For example, Fe₂O₃ is an *n*-type semiconductor under conditions where oxygen ion vacancies are formed along with electrons which tend to be localized on the cation sites. This is equivalent to forming a certain fraction of Fe²⁺ ions and increased conduction results. If Ti⁴⁺ is added to Fe₂O₃ in solid solution, an increased fraction of Fe³⁺ is forced into the Fe²⁺ state, equivalent to the Ti⁴⁺ additions. As a result, the conductivity of the product is substantially increased, ranging from 10⁻¹⁰ to 10⁻² (Ωcm)⁻¹ for Ti⁴⁺ concentration of zero to 0.5 atom %. Again, the conduction is determined primarily by the concentration of added titanium oxide and is much less dependent on oxygen partial pressure and firing conditions than is the pure material.

Tin oxide and indium oxide [1312-43-2], In₂O₃, are other important semiconductors that are doped to increase conductivity. SnO₂, In₂O₃, TiO₂, and in particular, SrTiO₃, are transparent to visible light and are often used as transparent electrodes, for example, on vidicon tubes.

TiO₂ as a semiconductor material is used as a gas sensor, and is sensitive to changes in environmental oxygen partial pressure. Whereas in the electrochemical sensor, ZrO₂-Y₂O₃, conduction is by oxygen ions, in TiO₂ sensors the conduction is by electrons (17). Pure TiO₂ has a band gap of 3.2 eV, and a fully occupied valence band (1,12). Therefore, at room temperature it is a highly resistive material. At elevated temperatures, dependent on oxygen partial pressures, it becomes oxygen deficient and Ti³⁺ ions are formed, to compensate for the anion deficiency, which contribute conduction electrons. As

more oxygen vacancies are created, the electron concentration increases and the resistivity of the material decreases. The resistivity of these materials is, therefore, highly dependent on temperature, energy of formation for the oxygen vacancies and on oxygen partial pressure, as shown in Figure 8 (17). This oxygen pressure dependence for many oxides is of the form: $\sigma = P_{O_2}^{\pm \delta}$ where $\delta = \frac{1}{8}$ to $\frac{1}{2}$. The sign of δ indicates *p*-type (+); or *n*-type (−) conduction.

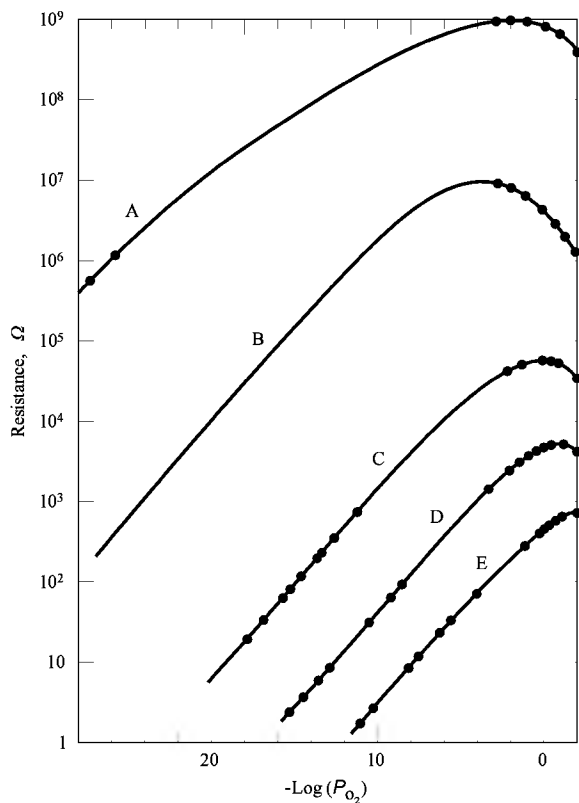


Fig. 8. Dependence of the resistance of TiO₂ ceramics on oxygen partial pressure in kPa. A, at 320°C; B, at 500°C; C, at 700°C; D at 850°C; and E, at 1000°C. To convert kPa to psi, multiply by 0.145 (17).

Another method of obtaining semiconductors having controlled resistivities, which avoids the difficulties caused by stoichiometric deviations, is the formation of solid solutions of two or more compounds having widely different conductivities. Magnetite [1317-61-9], Fe₃O₄, is an excellent conductor having a specific resistivity of about 10^{−4} Ωcm at room temperature, compared to values of about 10⁸ Ωcm for most stoichiometric transition-metal oxides. The high electrical conductivity of magnetite is a function of the random location of Fe²⁺ and Fe³⁺ ions on octahedral sites, allowing electron transfer from cation to cation. This is best illustrated by the order–disorder transformation occurring at about 120 K. Below this temperature the Fe²⁺ and Fe³⁺ ions are distributed in an ordered pattern on the octahedral sites. Above this temperature Fe²⁺ and Fe³⁺ positions become randomly distributed, resulting in a substantial increase in conductivity.

Spinels and Ferrites

The range of published values for the resistivity of ferrite and garnet [12178-41-5] materials is wide, from about 10^{−4} to 10⁹ ohmcm at room temperature (18,19). The low conductivity is typically associated with the simultaneous presence of Fe²⁺ and Fe³⁺ ions on equivalent lattice sites. Ferrite chemistry is complex and it is necessary to consider where the cations within the crystal locate as well as their type and concentration (20). In the spinel lattice, particular cations display a preference for one of several possible tetrahedrally or octahedrally coordinated lattice sites. The concentration and degree of preference for cations in the lattice modifies the site distribution of any specific cation. Ferrites should have very high electrical resistivities in order to eliminate eddy current and dielectric losses, and allow full penetration of electromagnetic fields throughout the solid (18,19). High resistivity is obtained when a cation has only one valence state in the lattice site. For the processing of these materials, high sintering temperatures and reducing atmospheres should be avoided. Such conditions produce mixtures of high and low valence cations.

The three main commercial classes of spinels are nickel–zinc, (NiZn)Fe₂O₄, manganese–zinc, (MnZn)Fe₂O₄, and magnesium–manganese ferrites, for example, (MnMg)Fe₂O₄. Electrical resistivity primarily determines the utility of these materials in the high megahertz or microwave frequency ranges. Lower frequency use requires a trade-off between high permeability and high resistivity. Nickel–zinc ferrites show an increase in permeability and a departure from stoichiometry in the iron-rich direction. Hence, a decrease in the resistivity results from making the formation of divalent iron more probable. Control of processing is, therefore, required to attain the most desirable properties.

Manganese–zinc and magnesium–manganese zinc ferrites are typically used in low frequency devices such as pulse transformers and for memory-core applications. As for the high frequency ferrite devices, these materials should also have high d-c resistivities for full magnetic penetration and low losses. High resistivities can be obtained by processing the oxide to be iron deficient. However, a more complex processing situation arises because of the three possible valence states of manganese and the site preference for each. Sintering temperature and cooling rate modify the manganese locations. Increasing the amount of manganese also increases the lattice constant, making it easier for magnesium ions to migrate and occupy both cation lattice sites. This migration is also accompanied by manganese movement such that divalent and trivalent ions are present on both sites, affecting the permeability, resistivity, and usage of the material (19,20).

Garnets have played an important role in the development of highly sophisticated microwave devices since the development of yttrium–iron garnet, yttrium iron oxide [12063-56-8]. The iron is strongly constrained to be trivalent in order to maintain electrical neutrality in the crystal, which is essential for low microwave losses. Garnets have lower values of saturation magnetization than spinels, but provide superior performance in microwave devices because they have a narrower resonance line width.

In general, a condition for appreciable conductivity in spinel structures is the presence of ions having multiple valence states on like crystallographic sites. The concentration of ions in Fe₃O₄ can be controlled by solid solutions in which Fe²⁺ or Fe³⁺ are diluted by other ions that do not participate in the electron exchange. Information regarding solid solutions of Fe₃O₄ and MgCr₂O₄, hercynite [1302-61-0], FeAl₂O₄, and ferrous chromite [1308-31-2], FeCr₂O₄ have been published (18). The temperature coefficient or activation energy increases with increasing resistivity. Semiconductor materials of this type, using materials like MgAl₂O₄, MgCr₂O₄, and titanium zinc oxide [12036-69-0], Zn₂TiO₄, as the nonconducting component, can be prepared using a controlled temperature coefficient of resistivity. Semiconductors made in this way are used as thermistors. Because the electrical conductivity has a negative

temperature coefficient (NTC), these materials are typically utilized in temperature sensors, controllers, and monitors.

Superconductivity

Oxide superconductors have been known since the 1960s. Compounds such as niobium oxide [12034-57-0], NbO, TiO, SrTiO_{3-x}, and AWO₃, where A is an alkali or alkaline earth cation, were found to be superconducting at 6 K or below. The highest *T_c* observed in oxides before 1986 was 13 K in the perovskite compound BaPb_{1-x}Bi_xO₃, *x* = 0.27. Then in 1986 possible superconductivity at 35 K in the La–Ba–Cu–O compound was discovered (21). The compound composition was later determined to be La_{1.85}Ba_{0.15}CuO₄. Work on the Y–Ba–Cu–O system was published in 1987 and reported a transition temperature above 90 K (22). This transition temperature was surpassed in early 1988 by the discovery of a series of bismuth-containing compounds, Bi–Sr–Ca–Cu–O, having the highest *T_c* = 100 K, and a Tl₂Ba₂CaCu₂O_{8-x} compound having a *T_c* = 120 K (23,24) (see BISMUTH COMPOUNDS).

Superconductivity is partly typified by a perfect metallic conductor that has no resistance to current flow below a critical transformation temperature (*T_c*). Besides the disappearance of electrical resistance, there is an expulsion of magnetic flux described as the Meissner effect. The BCS theory explains traditional superconductivity based on the concept of Cooper pairs. The electrons interact with phonons and attract each other, resulting in a lower combined energy less than the Fermi energy of the normal conduction electrons. The Cooper electron pairs move in the metal in such a way that at equilibrium the combined momenta are unchanged. Normal scattering effects, therefore, cause no effect on the forward momentum of the electron population accelerating in an electrical field. In spite of the success of the BCS theory for low temperature superconductors, the high temperature oxide superconductors do not conform well to the prediction of this model. Specifically, the BCS theory does not predict a *T_c* greater than 30 K or the existence of weak or no isotope effects.

The YBa₂Cu₃O_{7-x} compound is the most intensively investigated high temperature oxide superconductor. It has an oxygen deficient, distorted orthorhombic 1:1:3 (ABO₃) perovskite structure with *Pmmm* space group (25). The crystal structure shows the Y and Ba ions located in the center of the unit cell, Cu ions on the corners, and O ions on the edges. Based on neutron diffraction studies, the structure indicates two important features for Cu ions: (1) nonplanar CuO₂ planes extend in the crystallographic *ab* planes at *z* = 0.36 and *z* = 0.64, and (2) fence-like, square planar CuO₂ linear chains extending along the *b* axis at *z* = 0.

CuO₂ layers appear in all cuprate superconductors and appear to be a necessary but not sufficient condition for high temperature superconduction. The La₂SrCu₂O₇ compound has CuO₂ layers but does not superconduct. Experiments also indicate that *T_c* is proportional to the carrier density in the CuO₂ layer but not to the volume carrier density, which is further evidence that the YBa₂Cu₃O_{7-x} is a two-dimensional superconductor.

In these materials, the electrical conductivity and critical fields are highly anisotropic. Figure 9 shows this for highly oriented films and a single crystal in two directions (26). Conductivity in the *ab* (CuO) planes is metallic, whereas along the *c*-axis it is semimetallic. The conductivity can be greatly disturbed by defects such as vacancies and twin boundaries, in which the *a* and *b* axes are reversed, in particular by grain boundaries in the polycrystalline material. Because of the severe anisotropy, the critical current density is much higher in the plane than along the *c*-axis.

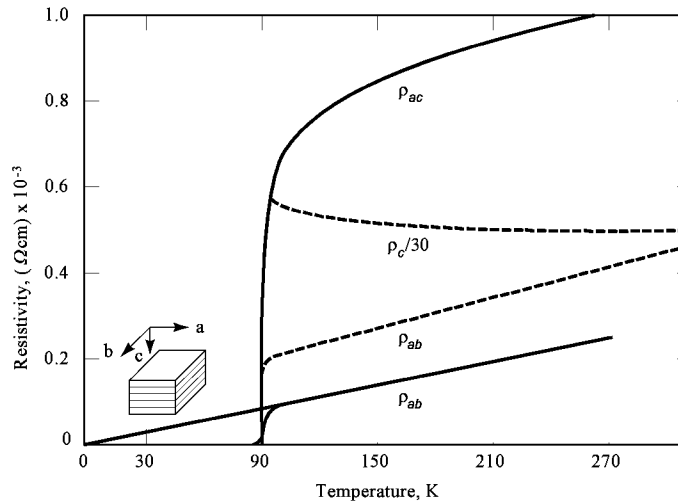


Fig. 9. Resistivity versus temperature showing onset of superconductivity for a single crystal (---) and for two highly oriented films (—), where ρ_{ab} denotes resistivity in the *ab* plane, ρ_{ac} in the *ac* plane, and $\rho_c/30$ represents 1/30 the resistivity in the *c*-direction to account for the much higher resistivity in this direction (26).

The YBa₂Cu₃O_{7-x} oxide superconductor is called an oxygen deficient perovskite because there are only seven oxygens per formula unit instead of the nine oxygens required for a perfect perovskite. The oxygen content in this compound is thus sensitive to processing and annealing conditions. When the *x* value is less than 0.5, an orthorhombic superconducting phase is present. As the compound loses oxygen and *x* becomes greater than 0.5, an order–disorder phase transition occurs and the structure transforms to a tetragonal phase having semiconducting characteristics. The tetragonal phase has a *P4/mmm* space group with oxygen disordered in the *z* = 0 plane as compared to the orthorhombic phase. There is a volume change of +0.2% associated with this phase transformation. Therefore, stresses are present resulting from the transformation and result in twin structure formation, usually observed along (110) reflection planes. The twin structure does not interrupt the continuity of the Cu–O superconducting planes, but does terminate the Cu–O chains between the Ba and Y planes.

The wide range of transition temperatures are found to depend on the presence of oxygen stoichiometry. The high transition temperature at 92 K in this compound can only be obtained when the oxygen content is between 6.8 and 7.0. Although *T_c* generally decreases as the oxygen content is reduced, the exact relationship is critically dependent on processing conditions. Applications for superconductors include magnetic resonance imaging for medical diagnostics (see IMAGING TECHNOLOGY), particle accelerators for experimental physics, and superconducting quantum interference devices (SQUID).

Ferroelectrics

A technologically important and often studied ceramic is ferroelectric barium titanate, BaTiO₃, which is the base for large volume production of disk and multilayer (MLC) capacitors. Barrier layer and intergranular capacitors (GBBL), as well as nonlinear positive temperature coefficient (PTC) resistors, are also largely based on this material. Ferroelectricity in these materials is a result of dipolar shifts in the cation lattice in going through a temperature transformation range, resulting in crystal symmetry changes and the development of spontaneous polarization charges. The spontaneous polarization structure consists of unipolar regions, or domains, which are randomly aligned so as to produce no net polarization in the absence of an applied field. Polar BaTiO₃ has a tetragonal structure (25–125°C) and a dielectric constant rising to a peak near the critical transformation temperature, ~125°C. Beyond this

critical temperature defined as the Curie temperature, T_c , the material becomes cubic and the spontaneous polarization disappears (1,6,7).

BaTiO_3 has an intrinsic high resistivity, $>10^{10} \text{ } \Omega\text{cm}$, when prepared in an oxidizing atmosphere. Through controlled doping of the A-site perovskite lattice using La^{3+} , Y^{3+} , or Nd^{3+} , or of the B-site using Nb^{5+} or Ta^{5+} semiconducting properties can be obtained (27). A complex defect structure arises as charge compensation mechanisms develop. At low concentration ($<0.3 \text{ mol } \%$), n -type conduction or electronic compensation results from the formation of donor Ti^{3+} ions (27,28). At high dopant concentration, the mechanism changes from electronic to ionic (oxygen $[\text{V}_{\text{Li}}]$ and or barium $[\text{V}_{\text{Ba}}]$ vacancies) compensation and the resistivity significantly increases (29,30). Low resistivities are obtained only within a very narrow dopant concentration range (0.1–0.3 mol %), as shown in Figure 10, which also shows a high dependence of the resistivity on temperature (31). Because of the formation of the Ti^{3+} ion in the doped BaTiO_3 , a local distortion of the Ti–O octahedron with associated change in the polarization field results. This gives a lowering of the $\text{Ti}(3d)$ energy level with a minimum in the energy associated with the Ti^{3+} state (16). The system, with a driving force dependent on dopant concentration, tends toward its lowest energy state. The mode of conduction in these materials results from polarization field overlap of local Ti^{4+} and Ti^{3+} discrete energy levels, with an associated lattice distortion caused by the electron movement and change in Ti-valency (9). This small polaron conduction occurs, therefore, as a result of the splitting of the $\text{Ti}(3d)$ orbitals and the associated polarization fields within the unit cells.

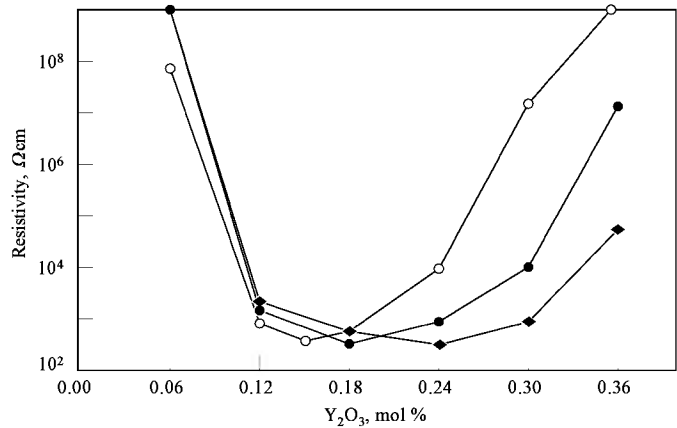


Fig. 10. Room temperature resistivity values of PTCR BaTiO_3 samples doped with Y_2O_3 as a function of mol % Y_2O_3 . Samples were annealed at 1220°C for 6 h and sintered for 2 h at (○) 1300°C ; (●) 1320°C ; and (◆) 1350°C (31).

Under controlled heat treatment, an insulating, thin, grain boundary barrier layer is formed in polycrystalline materials. In the grain boundary region oxygen is adsorbed during annealing, reducing the Ti^{3+} concentration within a thin region (12). Oxygen vacancies, likewise, diffuse from the interior and reside in the grain boundary region, acting as electron trap sites. A space charge or barrier layer is thereby produced as electrons move toward the grain boundary, which acts to repel the electron flow. At temperatures below the critical ferroelectric phase transition, low resistivity is found because of (+) spontaneous polarization charges neutralizing (-) grain boundary charges in crystallographically coherent areas along the grain boundaries, creating a low resistance path. Because of the ferroelectric, nonlinear behavior of BaTiO_3 , positive temperature coefficient of resistance (PTCR) characteristics are observed, manifested as a large increase in resistance by several orders of magnitude over a narrow temperature range, near the phase transition (29). This corresponds to a disappearance of the spontaneous polarization and a change in structure (27,28).

The PTCR effect is complex and not fully understood in terms of the grain boundary states and structure. Both the PTCR effect and room temperature resistivities are also highly dependent on dopant type and ionic radius. Figure 11 (32) illustrates this dependence where comparison of the PTCR behavior and resistivity are made for near optimum concentrations of La^{3+} , Nd^{3+} , and Y^{3+} ions separately substituted into BaTiO_3 . As seen, lowest dopant concentration and room temperature resistivity are obtained for the larger radius cation (La^{3+}), but the PTCR effect was sharpest for the smallest radius cation (Y^{3+}), reflecting dual site occupancy of the Y^{3+} ion.

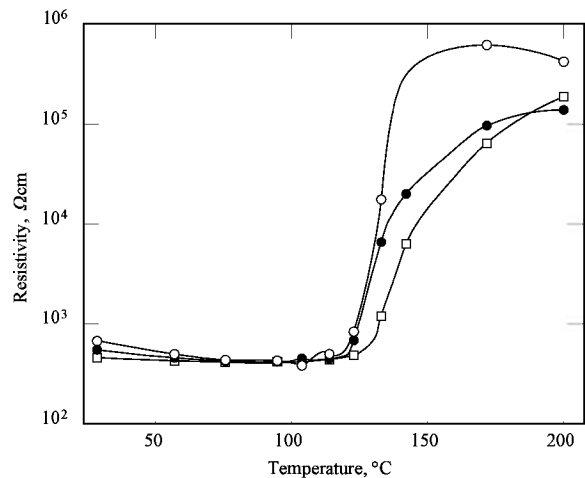


Fig. 11. PTC resistivity-temperature characteristics for donor dopants of (□) 0.15 mol La^{3+} ; (●) 0.15 mol Nd^{3+} ; and (○) 0.24 mol Y^{3+} in BaTiO_3 . Dopant concentrations are optimum amounts for each type. All were prepared as nitrates in the same manner (32).

By increasing the grain boundary thickness through the use of additional dopants, intergranular capacitors are obtained having high dielectric constants and low losses. These results are created by making the grain boundary barrier layer impassable as a large concentration of acceptor dopants nullify the effects of the spontaneous polarization, trapping the conducting electrons and creating a wide space charge layer, repelling all like charges. Several additional dopants, eg, Sr, Zr, Pb, Si, Cu, and Bi, to BaTiO_3 -based systems are used in the manufacture of both capacitor and PTC sensor devices, in order to adjust the temperature at which spontaneous polarization disappears and operating characteristics.

Certain perovskites with Pb on the A site are particularly important and show pronounced piezoelectric characteristics (PbTiO_3 , PZT, PLZT). Different responses are found in BaTiO_3 and PZT to the addition of donor dopants such as La^{3+} . In PZT, lead monoxide [1317-36-8], PbO , lost by volatilization during sintering, can be replaced in the crystal by La_2O_3 , where the excess positive charge of the La^{3+} is balanced by lead vacancies, leading to

compensation and no generated electronic charge carriers (33). This results in a marked increase in resistivity of the material.

Relaxors are ferroelectric materials which show a significant change in permittivity with frequency at temperatures near the Curie point, T_c . These materials also exhibit high permittivity values near T_c . Of particular interest for capacitors are the lead-based relaxors having the general formula $\text{Pb}(\text{B}_1\text{B}_2)\text{O}_3$, where B_1 is typically a low valence cation (Mg, Zn, Fe, Ni, or Sc), and B_2 is a high valence cation (Ti, Nb, Ta, or W). The best known relaxor is in the $\text{Pb}(\text{Mg}_{1/3}\text{Nb}_{2/3})\text{O}_3$ system (PMN), which shows excellent relaxor characteristics with a combined high dielectric permittivity and high resistivity.

These lead-based materials (PZT, PLZT, PMN) form a class of ceramics with either important dielectric, relaxor, piezoelectric, or electrooptic properties, and are thus used for applications in actuator and sensor devices. Resistive properties of these materials in film form mirror the conduction processes in the bulk material. Common problems associated with their use are low dielectric breakdown, increased aging, and electrode injection, decreasing the resistivity and degrading the properties.

Varistors

Varistors have a highly nonlinear current–voltage characteristic and are used to protect electronic equipment against voltage surges. Varistors are processed so as to develop a similar type microstructure to that previously described for PTC devices, where conductive grains are surrounded by thin insulating barriers (34). The actual operating mechanism is different however. At low voltages the grain boundary resistance is sufficiently high that little current leaks from the circuit. At the higher breakdown voltage, a tunneling process occurs, where the varistor responds very rapidly and allows the overvoltage pulse to be gated away from the device circuitry. The varistor resistance to ground decreases several orders of magnitude (Fig. 12). The above current density–voltage relationship can be described by a power law:

$$I = kV^\alpha \quad (1 < \alpha < \infty)$$

where I is the current through the device, V is the voltage, and the exponent α , which is a measure of device nonlinearity, is typically in the range 20–50. Ohmic-type behavior is found for low α values ($\alpha \sim 1$), whereas varistor behavior is quickly obtained for larger values of α . Figure 12 gives current density J versus applied field E for a typical varistor, as described by the slope $(1/\alpha)$ of the curve, where a large variation in current density is shown for a comparatively small change in field. The advantage of the ZnO varistor is the large obtainable α value.

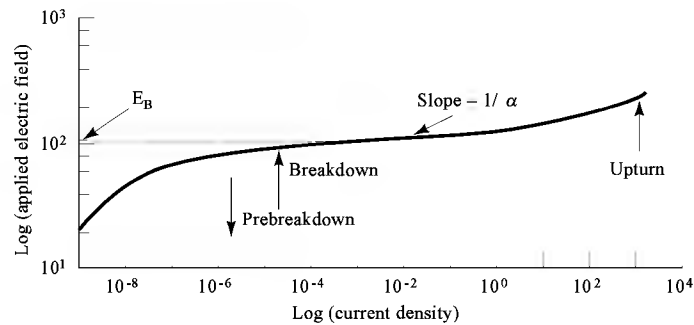


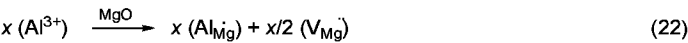
Fig. 12. Log–log plot of current density, J , versus applied electric field, E , for a ZnO varistor at room temperature, in which the breakdown field, E_B , is indicated. The exponent α equals the inverse slope of the curve, $\log(E/J) = 1/\alpha$, and is a measure of device nonlinearity. Units of current density and the electric field are A/cm^2 and V/cm , respectively (34).

To obtain these properties, polycrystalline ZnO is typically doped with antimony(III) oxide [1309-64-4], Sb_2O_3 , bismuth(III) oxide [1332-64-5], Bi_2O_3 , and other additives creating a highly complex oxide ceramic (34). The mechanism was first thought to be the result of a resistive Bi-rich second phase in the grain boundary. More recently, it is believed that the grains are separated by a thin adsorbed oxide layer which stores a negative charge equal in magnitude to the positive charged depletion layer, which lies wholly within each grain near the grain boundary. A barrier to electron flow at low voltages is created by these depletion regions. Transport through the grain junction is a compound step process. As the voltage increases, the depletion layer thins because there is a dramatic change in the conduction band shape and long-lived holes appear in the valence band. Electrons are able to tunnel through the interface because the tunneling barrier is now much thinner, and current flow is thereby greatly enhanced (34). Because the varistor action takes place across the ZnO grain boundaries, tailoring devices for specific breakdown voltages is done by fabricating the varistor with the appropriate number of grain boundaries in series between the electrodes.

Insulating Ceramics

Ceramic insulators are materials that do not pass a current when an electric field is applied, owing to the very low concentration of mobile charge carriers, electrons, or ions. These nonconducting materials are insulators. Important ceramic insulators such as SiO_2 , Al_2O_3 , mullite, BeO , AlN , boron nitride [10043-11-5], BN , and Si_3N_4 have resistivities $>10^{14} \Omega\text{cm}$. These high values are the result of a large energy gap between a filled valence band and the next available energy level, where the promotion of an electron into a higher state is energetically unfavorable. The conductivity of these ceramics is significantly influenced by both ionic and electronic defects.

In insulating oxides, ionic defects arise from the presence of impurities of different valence from the host cation. An aluminum ion impurity substituting in a magnesium oxide [1309-48-4], MgO , host lattice creates Mg vacancies,



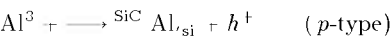
which can lead to ionic migration of Mg cations under the influence of an electric field. This is a high temperature process, however, and room temperature conductivities are still low ($<10^{-14} (\Omega\text{cm})^{-1}$).

Similarly, electronic conduction typically arises in these oxide materials from the natural loss of oxygen, which occurs in oxides on heating to high temperatures.



Electrons trapped at the vacancy can become partially or fully ionized, leading to weak n -type electronic conduction in an electric field. Again, the conductivity is low.

Conduction in materials such as AlN and SiC occur mainly through the presence of impurities having different valence states, leading to n - or p -type conduction.



(24)

$$\text{Si}^{4+} \xrightarrow{\text{AlN}} \text{Si}_{\text{Al}} + e' \quad (n\text{-type})$$

(25)

Similar conduction mechanisms can be expected for most nitride materials, including Si₃N₄ and BN. Depending on the level of impurity doping, SiC, which has only a moderate band gap (E_g = 2.8–3.2), can become semiconducting, with device possibilities and as heating elements. Electrically insulating SiC can also be fabricated using BeO dopant additions. This is an important material for laser heat sink applications because of its good thermal conducting and electrical insulating properties (see LASERS) (5).

The primary function of insulation in electrical circuits is the physical separation of conductors and the regulation or prevention of current flow between them. Ceramic insulators are used in many demanding applications where high electrical resistance is a requirement, together with other important properties such as thermal conductivity, high operating temperatures, high dielectric strength, low dielectric loss, resistance to thermal shock, environmental resistance, thermal expansion, and long-life characteristics. Insulators of this type are known as linear dielectrics. The dielectric constant is a measure of the ability of the material to store charge relative to vacuum and is a characteristic material property. In an a-c field, the electrical resistivity and dielectric constant are related by the dissipation factor, which measures the energy loss per cycle. This relationship is given by:

$$\sigma = \omega \epsilon_0 k' \tan \delta = \frac{1}{\rho}$$

(26)

where σ = conductivity; ρ = resistivity; ω = frequency ($2\pi f$); ϵ_0 = permittivity of vacuum (8.85×10^{-14} F/cm); k' = dielectric constant; $\tan \delta$ = dissipation factor; and $k' \tan \delta$ = dielectric loss factor = k'' .

The dielectric strength (DS) is a measure of the maximum voltage gradient that can be impressed across the dielectric without physical degradation of its insulating properties. Ceramics that satisfy the following property criteria at 25°C are classified as good insulators: $k' < 30$; $\rho > 10^{12}$ Ωcm; $\tan \delta < 0.001$; DS > 5.0 kV/mm; $k < 0.03$. These properties for several important dielectric ceramic insulators are given in Table 6.

Table 6. Dielectric Properties of Ceramic Insulators^a

Material	Molecular formula	Tan $\delta \times 10^{-4}$	Dielectric constant	Dielectric strength, kV/mm
porcelain	R ₂ O · Al ₂ O ₃ · SiO ₂	130	5.0–6.5	6.1–13.0
mullite	3Al ₂ O ₃ · 2SiO ₂	50	6.2–6.8	7.8
glass	Na ₂ O · CaO · SiO ₂	50	4.0–8.0	7.8–13.2
steatite	MgO · SiO ₂	20	6.0	7.9–13.8
alumina, 90–99%	Al ₂ O ₃	10	8.8–10.1	9.9–15.8
boron nitride	BN	10	4.2	35.6–55.4
beryllia	BeO	5	6.0	9.5–13.8
spinel	MgO · Al ₂ O ₃	4	7.5	11.9
quartz	SiO ₂	3	3.8–5.4	15–25
silicon nitride	Si ₃ N ₄	1	6.1	15.8–19.8
aluminum nitride	AlN	1	8.8	15
magnesia	MgO	1	8.9	8.5–11.0

^a Resistivity of all materials $> 10^{13}$ Ωcm at 25°C.

SiO₂ exhibits the lowest loss properties of any inorganic material. It is commonly used in insulating fibers and in the development of electrical porcelains (R₂O · Al₂O₃ · SiO₂). These materials have high dielectric strength with low loss and are therefore suitable for such high voltage applications as transmission line insulators, high voltage circuit breakers, and cutouts. Mullite, 3Al₂O₃ · 2SiO₂, MgO; and steatite, MgO · SiO₂, are extensively used for high temperature electrical insulation and for high frequency insulation because of low loss characteristics. Steatites are easily fabricated and have many applications; MgO is not as widely used because of difficulties in fabrication.

Al₂O₃ (see ALUMINUM COMPOUNDS, ALUMINUM OXIDE) is the most widely used oxide ceramic insulator, particularly as a substrate material for microelectronic devices and for use in severe conditions such as in spark plug insulation. Because of miniaturization and multilayer packaging of electronic devices, heat buildup is a primary concern. BeO, because of its very high thermal conductivity and good thermal expansion coefficient match to Si, is used when a high rate of heat dissipation is required, although its use is limited as a result of toxic effects. AlN, which combines high thermal conductivity with good thermal expansion match to Si, is under development as an alternative to BeO.

For electrical insulating sealing applications and heat sinks, Al₂O₃, AlN, SiC, and Si₃N₄ are the most commonly used materials. SiC and Si₃N₄ are also industrially valuable as high temperature heat exchangers because of high thermal conductivity and electrical insulating behavior, high hardness, durability, excellent high temperature, corrosion, and thermal shock resistance. Films of these materials, including diamond, are being developed, where the properties obtained are similar to that of the bulk materials. The conduction processes in the films mainly result from impurity and electrode injection effects, where the high resistivity and dielectric behavior become degraded.

Processing Effects

Most electrical ceramic properties are ultimately structure dependent. As indicated, stoichiometry is also very important, especially in ceramic materials having variable valence cations. Thus close control of composition, heat treatment temperature, and ambient atmosphere is needed in processing. Control of microstructure and grain size, particularly in magnetic ceramics, are also crucial to the attainment of desired properties. This is equally important in other categories of electrical ceramics, where density changes and the presence of additional phases can grossly affect properties. Heat treatment and thermal history during processing can affect properties in other ways as well. For example, in MgFe₂O₄ the distribution of cations between octahedral and tetrahedral sites is temperature dependent. The magnetic properties, which reflect this site occupancy are, therefore, strongly dependent on thermal treatment. In designing electrical ceramics for particular applications, therefore, processing parameters must be carefully monitored and controlled.

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CERAMICS, CHEMICAL WARE.

See CERAMICS.

CEREALS.

See WHEAT AND OTHER CEREAL GRAINS.

CERIUM AND CERIUM COMPOUNDS

Cerium [7440-45-1], Ce, at no. 58, is the most abundant member of the series of elements known as lanthanides. Lanthanide (Ln) is a collective name for the fifteen elements from at no. 57 (La) to 71 (Lu), also called the 4*f* elements. Rare-earth (RE) metal is the collective name for elements 21 (Sc), 39 (Y), plus 57 (La) to 71 (Lu). The label *light* is used herein for elements having atomic numbers from 57 to ~63 and the label *heavy* for numbers ~64 to 71.

Isolated first as an impure oxide in 1803, cerium was named after the earliest recognized asteroid Ceres. Cerium made its first contribution to chemical technology in the 1890s when, in Vienna, gas lights, using the Welsbach gas mantle based on a cerium-doped thorium oxide impregnated fabric, were introduced. Rapid widespread adoption of this form of illumination followed. Cerium still contributes to lighting in the 1990s but is now also to be found in automobiles, televisions, and other technologies.

Cerium, at wt 140.12; electron configuration [Xe] 4*f*⁶6*s*²; is characterized chemically by having two stable valence states, Ce³⁺, cerous, and Ce⁴⁺, ceric, for which the ionic radii are 114 pm and 97 pm, respectively. The easily accessible tetravalent ion is unique among the Ln series. Indeed, the ceric ion is a powerful oxidizing agent but when associated with the ligand oxygen, it is completely stabilized, and ceric oxide [1306-38-3], CeO₂, is the form of cerium most widely used. The most stable state for all lanthanides is a trivalent one, Ln³⁺, having an electronic configuration of [Xe]4*f*^{*n*}; ie, for Ce³⁺, [Xe]4*f*³. The 4*f* electrons are in well-shielded inner orbitals not influenced by surrounding atoms, and hence the chemical behavior of all Ln³⁺ ions is very similar. The relative increased stability of empty 4*f*⁰, half-full 4*f*⁷, and completely full 4*f*¹⁴ shells, however, can, for certain elements, cause oxidation states other than three to be reasonably stable. Ce⁴⁺ has a [Xe]4*f*⁰ configuration.

In bulk form cerium is a reactive metal that has a high affinity for oxygen and sulfur. It has a face centered cubic crystal structure, mp 798°C, bp 3443°C, density 6.77 g mL, and a metallic radius of 182 pm. Detailed chemical and physical property information can be found in the literature (1,2).

Cerium ranks ca 25th in abundance in the earth's crust (3), and cerium, which occurs at 60 ppm crustal abundance, not lanthanum at 30 ppm, is the most abundant lanthanide.

Resources

There are few principal lanthanide deposits, and there are no minerals that are sources for cerium alone. All the lighter lanthanides occur together in any potential deposit, and processes separating the lanthanides are necessary to obtain pure cerium products.

Whereas certain rocks of igneous origin formed by melting and recrystallization can include minerals enriched in the lanthanides (4), cerium is usually present as a trace element rather than as an essential component. Only a few minerals in which cerium is an essential structure-defining component occur in economically significant deposits. Two minerals supply the world's cerium, bastnasite [68909-13-7], LnFCO₃, and monazite [1306-41-8], (Ln,Th)PO₄.

Bastnasite, a light Ln fluoride carbonate, occurs in an unusual type of magma-derived alkaline igneous rock in which the concentration of the Ln elements has been especially enhanced. These carbonatite magmas are produced when mantle rocks melt deep in the earth's crust in the presence of large amounts of carbonate. If fluoride ion is introduced during the ascent, the final stage of the emplacement can be specific lanthanide-containing fluorocarbonate minerals such as bastnasite.

Bastnasite has been identified in various locations on several continents. The largest recognized deposit occurs mixed with monazite and iron ores in a complex mineralization at Baiyunebo in Inner Mongolia, China. The mineral is obtained as a by-product of the iron ore mining. The other commercially viable bastnasite source is the Mountain Pass, California deposit where the average Ln oxide content of the ore is ca 9% . This U.S. deposit is the only resource in the world that is minded solely for its content of cerium and other lanthanides.

Monazite, a light lanthanide thorium phosphate, is found in many countries. It is an accessory mineral in granites, and because of a high specific gravity, on weathering of those primary rocks the mineral segregates out as placer deposits. Monazite-bearing beach and dune sand deposits occur in association with other heavy minerals such as ilmenite [12168-52-4], FeO₃Ti, zircon, and rutile [1317-80-2]. The other minerals are usually the economic driving force for exploiting the deposits and hence monazite is almost always derived as a by-product.

Several countries supply monazite concentrates for the world market. Extensive deposits along the coast of western Australia are worked for ilmenite and are the primary source of world monazite. Other regions of Australia, along with India and Brazil, also supply the mineral. Because monazite contains thorium [7440-29-1], India and Brazil have embargoed its export for many years. In the United States, commerce in the mineral is regulated by the Nuclear Regulatory Commission.

Phosphate rock, mined widely throughout the world for its fertilizer value (see FERTILIZERS), in certain regions contains a few percent of lanthanides. For example, the apatite deposits in the Kola peninsula on the Russian Finnish border. The Ln content is recoverable from the various processing residues, and because other Ln-containing minerals, such as loparite [12173-83-0], are also found there, the location supplies a significant part of the demand in Eastern Europe.

World reserves of contained Ln oxide are estimated as 50,000,000 t with ca 75% of this in China, mostly at Baiyunebo, ca 15% in the United States, and ca 5% in India (5).

Production

The production of cerium derivatives begins with ore beneficiation and production of a mineral concentrate. Attack on that concentrate to create a suitable mixed lanthanide precursor for later separation processes follows. Then, depending on the relative market demand for different products, there is either direct production of a cerium-rich material, or separation of the mixed lanthanide precursor into individual pure lanthanide compounds including compounds of pure cerium, or both. The starting mineral determines how the suitable mixed lanthanide precursor is formed. In contrast the separation

technology, which involves liquid-liquid countercurrent extraction or solvent extraction (SX), for preparing the individual lathanides is essentially independent of the starting mineral (see [EXTRACTION, LIQUID LIQUID](#)). Thus different feedstocks can ultimately be processed by the same separation routines and equipment.

Processing of Bastnasite. In the United States the ore is extracted by open-pit mining and the bastnasite fraction is separated by froth-flotation from other minerals including barite, calcite, strontium-containing materials, and quartz. The resulting bastnasite concentrate is a commercially available commodity. A typical analysis is given in Table 1. Bastnasite can be converted directly, without separating out the individual Ln, to other derivatives by dissolution in acid, such as sulfate or chloride, ie, LnCl_3 , RECl_3 . Bastnasite-derived rare-earth chlorides [\[68188-88-5\]](#) have a composition very similar to the analogous material produced from monazite.

Table 1. Composition of Bastnasite Concentrate^a

Component	Composition, approx wt %
<i>Lanthanides</i>	
CeO ₂	30
La ₂ O ₃	20
Nd ₂ O ₃	7
Pr O ₁₁	2.4
other Ln	0.6
<i>Non-Lanthanides</i>	
SrO	5
CaO	4
BaO	1.5
F	5.5
SiO ₂	1.5
PO ₄	1
Fe ₂ O ₃	0.5
SO ₄	1

^a Loss on ignition (carbonate) is 20%.

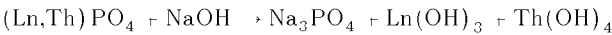
The step used in California to crack or open the concentrate for further processing is to roast in air, whereby Ce^{3+} oxidizes to Ce^{4+} , then leach with HCl to produce an insoluble cerium-rich portion, cerium concentrate [\[68909-12-6\]](#), and a soluble cerium-poor lanthanum-rich fraction.

A typical analysis of the insoluble cerium concentrate portion is by wt %; CeO₂, ~62; other Ln oxides, ~10; CaO, 6; other oxides, ~4; and F ~10. The loss on ignition is about 8 wt %. Cerium oxide readily takes F ions into the lattice. The charge difference is then matched by some Ln^{3+} replacing Ce^{4+} .

The soluble fraction from the HCl leach, after a simple SX removal of heavy lanthanides, is either converted to a solid lanthanum concentrate [\[68188-83-0\]](#) or used as the feedstock for further separation processes to produce pure light lanthanide derivatives. The lanthanum concentrate is essentially a mixed lanthanide hydroxide chloride where the total Ln oxides is 80 wt %, Cl is 12 wt %, and the loss on ignition is 8 wt %. This material contains a small (12 wt %) percentage of cerium as CeO₂, and because lanthanum concentrate is consumed in quantity in fluid catalytic cracking (FCC) catalysts for gasoline production, it accounts for a portion of the net consumption of cerium. La₂O₃ is present at 46 wt %; the remaining 22 wt % consists of other lanthanides.

An alternative process for opening bastnasite is used in China: high temperature roasting with sulfuric acid followed by an aqueous leach produces a solution containing the Ln elements. Ln is then precipitated by addition of sodium chloride as a mixed sulfate. Controlled precipitation of hydroxide can remove impurities and the Ln content is eventually taken up in HCl. The initial cerium-containing product, once the heavy metals Sm and beyond have been removed, is a light lanthanide (La, Ce, Pr, and Nd) rare-earth chloride.

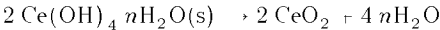
Processing of Monazite. Monazite, a by-product of the mineral-sands industry production of the economically more dominant minerals ilmenite, rutile, and zircon, is marketed worldwide as a concentrate in which the rare-earth oxide content is ~60%. The usual process to crack monazite is with alkali (6). After beneficiation, the monazite concentrate is finely ground and digested with an excess of caustic soda at ~150°C for several hours.



A soluble sodium tripolyphosphate is produced as are insoluble lanthanide and thorium hydroxides (hydrated oxides).

The solids are treated with hydrochloric acid at 70°C at pH 3–4. The thorium hydroxide [\[13825-36-0\]](#) remains insoluble and can be filtered off. Small amounts of trace contaminants that carry through into solution, such as uranium and lead as well as some thorium, are removed by coprecipitation with barium sulfate in a deactivation step. The resulting product, after SX-removal of the heavy Ln fraction, is a rare-earth lanthanide chloride, $\text{LnCl}_3 \cdot 6\text{H}_2\text{O}$. A typical analysis of this material gives from 22–25 wt % CeO₂, from 11–16 wt % La₂O₃, from 5–9 wt % Nd₂O₃, from 2–3 wt % Pr O₁₁, and from approximately 31 wt % chloride.

Production of Cerium Derivatives. Moderately pure (90–95%) cerium compounds can be made from rare-earth chloride through oxidation with, for example, hypochlorite to produce an insoluble cerium hydrate. The other lanthanides remain in solution. The hydrate, on calcination, converts to CeO₂.



The cerium concentrate derived from bastnasite can also be upgraded by dissolution and controlled reprecipitation.

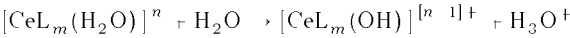
Ce(IV) extracts more readily into organic solvents than do the trivalent Ln(III) ions providing a route to 99% and higher purity cerium compounds. Any Ce(III) content of mixed lanthanide aqueous systems can be oxidized to Ce(IV) and the resulting solution, eg, of nitrates, contacted with an organic extractant such as tributyl phosphate dissolved in kerosene. The Ce(IV) preferentially transfers into the organic phase. In a separate step the cerium can be recovered by reduction to Ce(III) followed by extraction back into the aqueous phase. Cerium is then precipitated and calcined to produce the oxide.

Solvent extraction (SX) is also the process for the commercial separation of the individual light lanthanides (7). Each SX step, using nitrate or chloride solutions as the aqueous phase and kerosene as the organic phase and using chelating agents (qv) as extractants, cuts the Ln series into two parts. Consequently cerium can also be recovered from the second step in the general sequential SX processing of the Ln(III) series.

Cerium(IV) Chemistry

The fluorite structure, which has a large crystal lattice energy, is adopted by CeO₂ preferentially stabilizing this oxide of the tetravalent cation rather than Ce₂O₃. Compounds of cerium(IV) other than the oxide, ceric fluoride [\[10060-10-3\]](#), CeF₄, and related materials, although less stable can be prepared. For example ceric sulfate [\[13590-82-4\]](#), Ce(SO₄)₂, and certain double salts are known.

The tetravalent ceric ion [16065-90-0], Ce⁴⁺, is the only nontrivalent lanthanide ion, apart from Eu²⁺, stable in aqueous solution. As a result of the higher cation charge and smaller ionic size, ceric salts are much more hydrolyzed in aqueous solution than those of the trivalent lanthanides.



Ceric salt solutions are strongly acidic, basic salts tend to form readily, and there are no stable simple salts of weak acids.

The double salts, ceric ammonium nitrate [16774-21-3], (NH₄)₂[Ce(NO₃)₆], and ceric ammonium sulfate [19495-85-3], (NH₄)₂[Ce(SO₄)₃], are stable orange compounds prepared by dissolving freshly prepared hydrated oxide in excess of the appropriate acid and adding the correct amount of ammonium salt. Cerium(IV) is present in the anion, not the cation, of these salts. The crystal structure shows that the formal name should, for example, be diammonium hexanitratocerate. The solid sulfate analogues are correctly sulfatocerates. These complex anions and other similar species are stable in aqueous solutions. Chlorocomplexes of cerium(IV) are not as stable as nitrate or sulfato derivatives; the simple cerium tetrachloride [14986-52-8], CeCl₄, is unstable, because Cl⁻ is oxidized by Ce(IV), but salts of the hexachlorocerate ion [35644-17-8], [CeCl₆]²⁻, having large cations, do exist. Ceric salts range from yellow through orange to red in color, depending on the anionic form. Ceric ion in a glass matrix absorbs in the ultraviolet portion of the spectrum but not in the visible; the precise details of the spectra depend on glass composition.

Cerium in the tetravalent state is a strong oxidizing agent and can be reduced by, eg, oxalic acid, halogen acids, ferrous salts, and hydrogen peroxide. The exact oxidation potential for the one-electron reaction of Ce(IV) to Ce(III) ranges from ca 1.3 V in 1 N HCl to ca 1.8 V in 6 N HClO₄ and it depends on which small anionic groupings are complexed to the tetravalent cerium. Aqueous solutions containing Ce(IV) species are stable, despite the lower electrode potential for the H₂O/O₂ couple (1.23 V), probably for kinetic reasons. Cerium(IV) oxidation is a valuable tool in organic chemistry (8) and can be used for quantitative volumetric oxidation reactions called cerate oxidimetry in analytical chemistry (9).

Cerium Oxide. The most stable oxide of cerium is cerium dioxide [1306-38-3], CeO₂, also called ceria or ceric oxide. When cerium salts are calcined in air or if oxygen is present, this tetravalent Ce(IV) oxide is formed, cerium sesquioxide [1345-13-7] Ce₂O₃, can be prepared in strongly reducing conditions but is unstable in air and water, readily converting to the dioxide. Cerium has one of the highest free energies of formation for an oxide. The dioxide is soluble in mineral acids but can prove difficult to dissolve unless a trace of reducing agent such as hydrogen peroxide is added.

Ceria has the fluorite (CaF₂) structure having eight-coordinate cations and four-coordinate anions. Under some circumstances it can exhibit large deviations from stoichiometry giving CeO_{2-x}, where x can be up to 0.3. The color of the oxide is sensitive not only to stoichiometry but also to the presence of other lanthanides. Pure CeO₂ is a very pale yellow but a slight trace (ca 0.02 wt %) of Pr results in a buff color attributable to Ce(IV)–Pr(III) transitions. Grossly nonstoichiometric ceria samples are reported to be blue.

Solid solutions of ceria with trivalent ions, eg, Y and La, can readily be formed. The M³⁺ ions substitute for the tetravalent Ce and introduce one oxygen vacancy for every two Ln³⁺ ions. The dopant ions and the oxygen vacancies form charge associates. The resulting defect-fluorites have good oxide ion conductivity and are novel solid electrolytes for temperatures above ~600°C (10).

Cerium(III) Chemistry and Compounds

Cerium is strongly electropositive having a low ionization potential for the removal of the three most weakly bound electrons. The trivalent cerous ion [18923-26-7], Ce³⁺, apart from its possible oxidation to Ce(IV), closely resembles, the other trivalent lanthanides in behavior.

The simple cerous salts can be prepared by dissolving the oxide, or preferably a more reactive precursor, in the appropriate acid or, when possible, produced by precipitation from solution. Upon crystallization a wide variety of hydrated species can result. These hydrates tend to be hygroscopic. Basic salts, eg, Ce(OH)CO₃, may be formed and these can be contaminants in the solid salts.

Ce(III) forms a water-insoluble hydroxide, carbonate, oxalate, phosphate, and fluoride; sparingly soluble sulfate and acetate; and soluble nitrate and chloride (and bromide). In solution the salts are only slightly hydrolyzed. The carbonate is readily prepared and is a convenient precursor for the preparation of other derivatives. The sparingly soluble sulfate and acetate decrease in solubility with an increase in temperature. Calcination of most Ce(III) salts results in CeO₂.

Cerous salts in general are colorless because Ce³⁺ has no absorption bands in the visible. Trivalent cerium, however, is one of the few lanthanide ions in which parity-allowed transitions between 4f and 5d configurations can take place and as a result Ce(III) compounds absorb in the ultraviolet region just outside the visible.

Hydroxide. Freshly precipitated cerous hydroxide [15785-09-8], Ce(OH)₃, is readily oxidized by air or oxygenated water, through poorly defined violet-tinged mixed valence intermediates, to the tetravalent buff colored ceric hydroxide [12014-56-1], Ce(OH)₄. The precipitate, which can prove difficult to filter, is amorphous and on drying converts to hydrated ceric oxide, CeO₂·2H₂O. This commercial material, cerium hydrate [23322-64-7], behaves essentially as a reactive cerium oxide.

Carbonate. Hydrated cerous carbonate, Ce₂(CO₃)₃·*n*H₂O when prepared under ideal conditions tends to crystallize as cerous carbonate octahydrate [16545-92-5], *n* = 8. The commercial product, prepared on a large scale by sodium carbonate addition, has a composition best represented as cerous carbonate trihydrate [64360-90-3], *n* = 3. Several other hydrates are known.

Temperature, pH, precipitation conditions, and the drying process determine the amount of water in the solid. In addition the species Ce(OH)(CO₃)·*x*H₂O and Ce₂O₂(CO₃) may also be present. Thermal decomposition causes loss of crystallization water followed by the formation of ill-defined hydroxy- and oxy-species and eventually, at ~550°C, CeO₂. Discrete intermediates are not seen because of the concomitant oxidation of Ce(III) to Ce(IV).

Nitrate. Cerium(III) nitrate hexahydrate [10294-41-4], Ce(NO₃)₃·6H₂O, is a commercially available soluble salt of cerium, and because of ready decomposition to the oxide, it is used, for example, when a porous solid is to be impregnated with cerium oxide. The nitrate is very soluble in water, up to about 65 wt %. It is also soluble in a wide range of polar organic solvents such as ketones, alcohols, and ethers.

Halides. Cerous chloride hydrate [19423-76-8], CeCl₃·*n*H₂O, usually with *n* ~ 6, on heating tends to form cerous oxychloride [15600-64-3], CeOCl. The anhydrous cerous chloride [7790-86-5] can be made from the hydrated salt by suppressing oxyhalide formation during thermal dehydration by the presence of hydrogen chloride or ammonium chloride. The anhydrous salt is soluble in a variety of organic solvents, eg, alcohols and ethers, has mp 817°C, and can be volatilized at high temperatures in vacuum.

Precipitation of cerous fluoride [7758-88-5], CF₃, from aqueous solution by HF addition produces CeF₃·*n*H₂O, *n* ~ 1₂, from which the anhydrous salt can be prepared by controlled dehydration. CeF₃, mp 1432°C, can also be prepared by reaction of a suitable precursor, such as carbonate, and ammonium bifluoride, NH₄HF₂. The anhydrous chloride and fluoride are potential precursors for cerium metal production. Cerous oxyfluoride [20901-12-6], CeOF, materials have novel ionic conductivity. The oxyfluoride and oxychloride are both high melting species that often form during halide salt calcination.

Carboxylates. Cerium carboxylates, water-insoluble, can be made (11) by double decomposition and precipitation using water-soluble precursors, or by reaction of an insoluble precursor directly with the organic acid. Cerous oxalate [139-42-4], Ce₂(C₂O₄)₃, 2-ethylhexanoate (octanoate), naphthenate, and stearate are readily prepared.

Sulfides. Several cerium sulfides have been characterized (12) including the expected cerium(III) sulfide [12014-93-6], Ce₂S₃. Cerium monosulfide [12014-82-3], CeS, and tricerium tetrasulfide [12185-95-4], Ce₃S₄, are also known. CeS (13), bronze in color with a metallic lustre, adopts the NaCl structure with the ions Ce³⁺, S²⁻, and one electron in a conduction band. This sulfide has a high (in the metallic range) electrical conductivity, a high thermal conductivity, a high (ca 2715 K) melting point, and good thermal shock resistance.

Cerium(III) oxysulfide [12442-45-4], Ce₂O₂S, is a high melting stable compound that precipitates out when steel is treated with a cerium-based metal

to control sulfide inclusions. Its thermodynamic properties are well known and the Ce–O–S phase diagram has been determined (14).

Miscellaneous Compounds. Among simple ionic salts cerium(III) acetate [17829-82-2] as commercially prepared, has ~1¹ ₂ H₂O, has a moderate (~100 g L) aqueous solubility that decreases with increased temperature, and is an attractive precursor to the oxide. Cerous sulfate [13454-94-9] can be made in a wide range of hydrated forms and has solubility behavior comparable to that of the acetate. Many double sulfates having alkali metal and or ammonium cations, and varying degrees of aqueous solubility are known. Cerium(III) phosphate [13454-71-2], being equivalent to monazite, is very stable.

Derivatives such as borides, carbides, nitrides, and hydrides are best prepared by direct reaction between the elements. These metalloid-type compounds, which often show variable composition, are colored and sometimes semiconducting.

Metal

In bulk form cerium is a reactive metal. Pure metal is prepared by the calciothermic reduction of CeF₃.



A slight excess of calcium is used and the exothermic reaction, carried out in a tantalum crucible, is initiated at ~900°C. After physical separation of the upper layer of immiscible fluoride slag, vacuum distillation removes unreacted volatile Ca. Cerium can also be made by the electrolytic reduction of fused chloride.

On a fresh surface the metal has a steely lustre but rapidly tarnishes in air as a result of surface formation of oxide and carbonate species. For protection against oxidation the metal is usually stored in a light mineral oil. When made finely divided, eg, on being cut, it can be strongly pyrophoric, and, for this reason is used, as the ferro-alloy mischmetal, in lighter flints and ordnance. Cerium reacts steadily with water, readily dissolves in mineral acids, and is also attacked by alkali; it reacts with most nonmetals on heating.

Cerium metal has unique solid-state properties and is the only material known to have a solid–solid critical point. Three allotropes, α, β, γ, are stable at or close to ambient conditions and have complex structural interrelationships.

Mischmetal. Mischmetal [62379-61-7] contains, in metallic form, the mixed light lanthanides in the same or slightly modified ratio as occurs in the resource minerals. It is produced by the electrolysis of fused mixed lanthanide chloride prepared from either bastnasite or monazite. Although the precise composition of the resulting metal depends on the composition of chloride used, the cerium content of most grades is always close to 50 wt %.

An alternative commercial form of a metallic mixed lanthanide-containing material is rare-earth silicide [68476-89-1], produced in a submerged electric-arc furnace by the direct reduction of ore concentrate, bastnasite, iron ore, and quartz. The resulting alloy is approximately 1/3 mischmetal, 1/3 silicon, and 1/3 iron. In addition there are some ferro-alloys, such as magnesium–ferrosilicons, derived from cerium concentrate, that contain a few percent of cerium. The consumption of metallic cerium is overwhelmingly in the mixed lanthanide form in ferrous metallurgy.

Analysis

Preliminary separation of the lanthanides as a complete group is often possible by oxalate precipitation at low pH. In most cases direct calcination, at ~1000°C, of oxalate to the oxide provides a gravimetric determination of total Ln oxide content. If necessary controlled hydroxide precipitation can reject alkaline earths. The Ln oxide can be redissolved in strong acid and titrated against EDTA or other complexing agents. Depending on analytical procedures and on the sample it may be necessary to ensure that all the Ce is in one oxidation state, eg, 3+, by using a reducing agent such as ascorbic acid. The ceric content can be determined by oxidation of Ce³⁺ to the tetravalent state by persulfate or bismuthate then titrating the resulting Ce⁴⁺ with standard ferrous ammonium sulfate. Qualitative colorimetric tests are also possible.

Several instrumental methods are available for quantitative estimation of from moderate to trace amounts of cerium in other materials. X-ray fluorescence is widely available, versatile, and suitable for determinations of Ce, and any other Ln, at percent levels and lower in minerals and pure materials. The uv-excited visible luminescence of cerium is characteristic and can be used to estimate Ce content, at ppm levels, in a nonluminescing host. X-ray excited optical luminescence (15), a technique especially appropriate for Ln elements including cerium, relies on emissions in the visible, and also measures ppm values. Atomic emission spectrometry is applicable to most lanthanides, including Ce (16). The precise lines used for quantitative measurement must be chosen with care, but once set-up the technique is suitable for routine analyses.

Biological and Toxicological Behavior

In general the lanthanides, including cerium, have a low toxicity rating (17), especially when they are present in material having low aqueous solubility. When orally administered poor absorption from the gastrointestinal tract tends to result in the lanthanides generally having little effect. The anion is often an important determinant in toxicity.

Historically the use of monazite, a thorium-containing mineral, as the principal lanthanide resource led to confusion regarding the relation between radioactivity and the lanthanides. Inadequate separations produced Th-contaminated Ln products. Modern processing technology results in products that meet all regulatory requirements.

Economic Aspects

The yearly worldwide production of lanthanides is nearly 70,000 tons (18) measured as contained Ln oxide. The primary sources are given in Table 2. For finished products the principal supplying companies are Molycorp (United States), Rh ne-Poulenc (France), several Japanese companies, such as Mitsubishi, Santoku, and Shinetsu, and some Chinese organizations. The rise of Chinese lanthanide production during the 1980s has become a significant factor in the global market picture.

Table 2. 1990 Lanthanide Production, t^a

Australia	7,500
Brazil	2,500
China	25,000
India	2,000
Malaysia	2,000
United States	21,000
former USSR	8,000

^a As contained Ln oxide, wt approximate.

Cerium is used in several forms other than as the pure oxide. Only a small fraction of the 70,000 ton Ln total is produced as separated, relatively pure individual Ln derivatives, cerium included. The bulk of the material is consumed as concentrates, cerium included.

The various cerium-containing derivatives available commercially are summarized in Table 3. The 1991 prices, per kg of contained Ln oxide, ie, not necessarily Ce oxide, range from about \$3 for types A and B, ca \$5 for type C, ca \$12 type D, and ca \$25 for type E.

Table 3. Commercially Available Cerium-Containing Materials and Uses

Type	Material	Use	Cerium content
A	rare-earth chloride, mischmetal	FCC ^a catalysts iron metallurgy	principal component ^b
B	lanthanum concentrate, La–Ln chloride	FCC ^a catalysts	minor component ^b
C	cerium concentrate	glass polishing, glass decolorizing	dominant element ^c
D	oxide, nitrate, metal	autoemission catalysts, etc	> ca 90 wt %
E	oxide, salts	luminescence, catalysts	> ca 99 wt %

^a FCC – fluid catalytic cracking
^b Of mixed-lanthanide composition.
^c In oxide-type compound.

Uses

The technological applications of cerium rely predominantly on its high thermodynamic affinity for oxygen and sulfur, potential redox chemistry involving cerium(III) and cerium(IV), and the absorption – excitation energy bands associated with its electronic structure. Uses may be categorized as occurring in metallurgy (qv), glass (qv) and ceramics (qv), catalysis (qv), and chemicals, plus phosphors – luminescence.

The purity of the cerium-containing materials depends on the application as indicated in Table 3, and purity can mean not only percentage of cerium content but also absence of unwanted components. For some uses, eg, gasoline production catalysts, the lanthanides are often used in the natural-ratio without separation and source literature for these applications often does not explicitly mention cerium. Conversely, particularly in ferrous metallurgy, cerium is often assumed to be synonymous with rare-earth or lanthanide and these terms are used somewhat interchangeably.

Metallurgical Applications.

Steel. Mischmetal (MM) and other cerium-containing ferro-alloys are used to improve the physical properties of high strength – low alloy (HSLA) steels (19). Cerium is added primarily to provide sulfide shape control but also as a deoxidizer or desulfurizer because steel quality is improved when the oxygen and sulfur content is minimal. Nonmetallic inclusions, particularly of certain sulfides, can deform at high working temperatures. These platelike inclusions produce layers of weakness and hence undesirable mechanical properties in the final steel. When added to the molten steel, cerium and other lanthanides combine avidly with oxygen and sulfur, even reducing other oxides and sulfides originally present, to form high melting, hard Ln oxysulfides and oxides, which do not deform later during rolling of the steel. In addition these same inclusions can provide nuclei during solidification that promote a fine-grained final product.

Modern steelmaking technology, with an emphasis during production on low levels of oxygen and sulfur, results in cleaner steels. This, together with the general downturn in steel production in the western economies, has resulted in a significantly reduced demand for mischmetal in the steel industry. In contrast, in China, which has abundant Ln reserves and less advanced steelmaking technology, mischmetal consumption in steel treatment amounts to about 75% of their Ln production.

Cast Iron. Cast irons contain carbon (qv) as the main alloying element, are heterogeneous in microstructure, and form an extensive family of materials that includes gray iron, compacted graphite, and ductile iron. The key to obtaining distinctive differences in properties between individual cast-iron types is the control of the carbon content and especially control of the morphology that graphitic carbon precipitates assume in the final product. Crystal morphology depends on tramp elements bound to the growing crystallite surfaces.

The lanthanides, and in particular cerium, are used (20) to provide this graphite morphology control, for example to produce spherulitic or vermicular crystallites. The elements are usually added as silicides or in various ferro-alloys with cerium as the principal lanthanide. The function of cerium and all the lanthanides is probably to remove free oxygen and sulfur from the melt through formation of stable lanthanide oxysulfides, akin to the role in steel technology; to initiate the special carbon crystal growth by nucleation on those oxysulfide compounds; and to tie up undesirable tramp elements, eg, Pb and Sb, as intermetallics.

Lighter Flints and Getters. Traditionally the item most widely associated with cerium has been the pyrophoric iron-mischmetal (~60%) alloy for lighter flints, in limited use in the 1990s. Similar low vapor pressure reactive alloys based on cerium, such as Th₂Al-MM, can also be used as getters for electronic equipment and vacuum tubes (see ELECTRONIC MATERIALS; VACUUM TECHNOLOGY).

Super Alloys. Super alloys are nickel- or cobalt-based alloys that are exceptionally heat-resistant and are used, for example, in gas turbine engines in aircraft (see COBALT AND COBALT ALLOYS; NICKEL AND NICKEL ALLOYS). One operating problem, caused by the repetitive cycling from ambient up to high temperature, is the tendency for the essential protective oxide skin on the metal surface to spall off. Several commercial alloys have ~0.05 wt % pure cerium that significantly improves this oxidation resistance, provides creep resistance, and confers a longer operating life (21). This alloy property improvement probably comes from the trapping of trace unwanted sulfur impurities from the metal crystallite boundaries plus a modification to the diffusion mechanism for oxide skin growth. The oxide skin formed at high temperatures shows less tendency to spall off when cerium is present in the alloy.

Aluminum Alloys. Aluminum alloy systems, under development for use at higher temperatures than is normally possible with aluminum, can be made by rapid solidification powder metallurgy processes (see ALUMINUM AND ALUMINUM ALLOYS; HIGH TEMPERATURE ALLOYS). The novel compositions produced have additive element concentrations, eg, of cerium, beyond those possible using conventional ingot metallurgy. One of the most promising of the lightweight alloys is an Al-8.3Fe-4.0Ce (wt %) material, having excellent properties in the 230°C to 340°C range (22).

The technique of rapid solidification enables relatively large amounts of insoluble metallic elements to be finely dispersed within atomized powders. Upon freezing very small intermetallic particles are formed, resulting, after further processing, in a high volume fraction of finely dispersed particles within the aluminum matrix and hence a dispersion strengthened alloy. The intermetallic phases, or possibly oxidic species, responsible for the dispersion strengthening are probably binary Al-Fe and ternary Al-Fe–Ce compounds.

Chromium Plating. Chromium is deposited onto many consumer articles and industrial items to provide decoration as well as corrosion resistance. The chromium coating is produced by an electroplating (qv) process from an aqueous solution containing a chromium salt. Chromium cannot easily be plated directly from Cr(III), however, because of the high stability of the aquo-ion [Cr(H₂O)]³⁺. It needs to be present as Cr(VI), which can be reduced to Cr(O), ie, chromium metal, through the intermediary of a protected Cr(III) species avoiding the formation of the stable hexaquo-chromium(III) ion. The plating solutions must contain an anion, such as fluoride, to stabilize the active Cr(III) intermediate and prevent the aquo-ion from forming. It has proved difficult to maintain a stable F[–] concentration. The addition of cerous ions, Ce³⁺, as cerium fluoride added directly to the plating bath, gives a self-regulating electrolyte (23). The solubility of cerous fluoride is nearly independent of the temperature of the plating solution within the practical range. By ensuring that excess, undissolved CeF₃ is always present, the fluoride ion concentration can be closely controlled and quality plating achieved.

Welding Electrodes. The electrodes used in certain welding (qv) technologies, such as inert gas tungsten-arc welding, contain a finely dispersed oxide distributed throughout the tungsten matrix. These oxide particles give an arc-strike reliability to the electrodes at lower voltages than tungsten alone can provide. Cerium oxide, at 2 wt % loading, provides an alternative to thorium oxide, a common additive that is being phased out for environmental reasons (24).

Glass and Ceramic Applications.

Glass Polishing. The most efficient polishing agent for most commercial glass compositions is cerium oxide (25). This application consumes, either as a moderately pure oxide or as a cerium oxide-dominated concentrate, a significant portion of the cerium products produced annually. Commercial glass polishes (qv) are based on cerium oxide powders having defined particle sizes and controlled dispersibility in aqueous systems. The polishing process requires water, and it is a softer hydrated surface layer that is removed or reformed. In general, the polishing agent should have a Mohs' hardness of ~6.5, close to the hardness of most glasses. Cerium oxide slurried in water contains the potential polyvalent cerium atom, and redox reactions from the

Ce(IV)–Ce(III) couple may well provide chemical assistance in breaking up the silicate lattice. Transient formation of complexed groupings consisting of ..Ce-O-Si.. has been suggested.

The cerium concentrate derived from bastnasite is an excellent polish base, and the oxide derived directly from the natural ratio rare-earth chloride, as long as the cerium oxide content is near or above 50 wt %, provides an adequate glass polish. The polishing activity of the latter is better than the $\text{CeO}_2\text{:LnO}$ ratio suggests. Materials prepared prior to any Ln purification steps are sources for the lowest cost polishes available used to treat TV face plates, mirrors, and the like. For precision optical polishing the higher purity materials are preferred.

Glass Decolorization. An important use for cerium compounds is the decolorization of glass. The dominant glass produced is the soda lime-type made from inexpensive raw materials, the purity of which determines the color of the finished product. One common impurity from silica sand, iron, is a moderately strong colorant in glass and as little as 0.01 wt % can be visually detected. The coloration caused by iron results from absorption of both the ferric and ferrous ions. Glass can be decolorized without changing the total iron content by keeping all the iron in the Fe^{3+} state by addition of Ce^{4+} to the glass bath.

Cerium(IV) oxidizes ferrous ion to ferric and the cerium ions are stable under the conditions of a molten silicate–glass bath. Furthermore, cerium itself has no absorption in the visible region. Economical additions of cerium, as cerium concentrate, enable the efficient use of raw materials containing trace quantities of iron (26).

Ultraviolet Absorption. The damage sunlight causes materials from near uv (300–400 nm range) radiation, can be limited by screening out the damaging radiation through the incorporation of components that absorb at those wavelengths. Cerium(IV) in particular makes glass opaque to near uv radiation but shows no absorption in the visible; cerium(III) has similar behavior (27). Cerium-doped glass has applications in several areas, eg, medical glassware, display case glass windows, etc.

The photostability of pigments can be enhanced by surface additives that increase the provision of recombination centers for the photoproduced charge carriers that would otherwise cause chemical damage. The surface additive must be a one-electron redox couple and be present in both valence states. Cerium, through the Ce(III)–Ce(IV) interconversion, can provide this protective process, giving pigments lightfastness. The rate at which certain pigments, such as titanium dioxide, darken on exposure to light can be reduced by producing a precipitated cerium salt coating on the pigment particles (28).

Radiation-Resistant Glass. Television glass faceplates are subjected to electron bombardment by high energy electrons, particularly with the high tube voltages needed for color displays. Over time this bombardment causes discoloration or browning of the glass because of the creation of color centers, an effect which is suppressed by the addition of up to 1 wt % or so of cerium oxide to the glass. A similar suppression of gamma-ray induced discoloration is also possible and cerium-containing glasses are used in the construction of viewing windows in hot-cells in the nuclear industry. The suppression mechanism in both instances is believed to depend on the presence of both Ce^{3+} and Ce^{4+} ions within the glass lattice (29).

Photo-Sensitive Glass. On exposure to strong light, certain glass formulations develop a latent image that can, in a later step, be converted into a permanent structural or color change. This type of glass contains cerium ions that absorb ultraviolet radiation and release electrons into the glass matrix. Heat treatment causes these electrons to migrate to silver ions, also present, that initially form silver specks that in turn nucleate the crystal growth of other compounds within the glass (30). Highly detailed patterns can be produced that are not only decorative but also can help create masks, spacers, and the like for electronic uses.

Opacifier in Enamels. Cerium oxide has a high (~2.2) refractive index and is a potential opacifying agent (31) in enamel compositions used as protective coatings on metals. In addition to a high thermal stability, ceria has only one crystallographic form throughout the range of temperatures met during enameling. Opacity in porcelain enamels refers to the desired white cover-coat surface and is created when the opacifier, the oxide, precipitates out as micrometer-sized crystals during the firing on of the enamel (see ENAMELS, PORCELAIN, OR VITREOUS).

Zirconia Ceramics. Zirconia, ZrO_2 , the high temperature engineering ceramic, needs an additive to produce components having high strength and toughness (see ADVANCED CERAMICS). A so-called phase stabilizer is added in order to maintain a portion of the ZrO_2 as dispersed particulates of the tetragonal phase within the matrix cubic phase at ambient temperatures. Addition of ~12 mol % of CeO_2 , for example, to zirconia produces a material having exceptional toughness and good strength (32,33). Cerium oxide-doped zirconia is also used in thermal barrier spray coatings on metal surfaces (34) such as aircraft engine parts in order to reduce the high temperatures to which the metal substrate would be exposed (see METAL SURFACE TREATMENTS).

Optical Coatings. Thin surface coatings are applied to optical components to improve performance. Wideband antireflection coatings for the visible and ir regions need materials with a refractive index of ~1.5 for the best efficiency. Cerium fluoride, a stable material resistant to humidity damage, has a suitable index, 1.63 in the visible, 1.59 in the infrared, and is transparent over the range 0.5 μm to 5 μm . It is one of the compounds used to build up the multilayers deposited on lenses, sensors, and the like.

Catalytic and Chemical Applications.

Cracking Catalysts. Several catalysts used to convert crude oil to lower molecular-weight fractions, such as gasoline, contain lanthanides including cerium (35). Within the United States alone ~500 tons of FCC are consumed per day. An FCC unit has a lower reactor temperature and a higher regenerator temperature; the catalyst circulates between the two. FCC catalysts contain crystalline zeolites and additives embedded in an inert matrix. The zeolite, a special aluminosilicate with organic molecule-sized pores, requires cations within those pores for charge neutrality, to give catalytic reactivity in the reactor and to provide thermal stability in the regenerator.

Large highly charged ions, such as La^{3+} or Ce^{3+} , bound within the zeolite pores create a high electric field gradient strong enough to dissociate adsorbed water and provide a high surface acidity. The Ln content can reach up to 10 wt % or higher by weight of the zeolite, but not all FCC catalysts contain lanthanides. Catalysts with a range of Ln content are made, each designed to meet specific refinery needs. Cerium, because of the potential availability of the Ce^{4+} state that tends to hydrolyze at the ion-exchange pH used, is often partially removed from the precursor solutions.

The lanthanides, be they La, Ce, or others, are used to give high cracking activity to the catalysts, especially to produce low octane fuel from heavy crude oil feedstocks. Consumption of lanthanides, and hence of cerium, in FCC catalysts has altered during the decade of the 1980s because of increased demand for high octane fuels, greater feedstock availability of lighter crudes, and changes in catalyst technology. FCC Ln demand reached a peak in ~1984 when one-third of all Ln consumption was in FCC.

This trend has influenced the supply and availability of cerium, particularly in comparison to the availability of lanthanum-rich cerium-poor materials. The increase in Ln demand for FCC catalysts up to the mid-1980s, together with the need to separate out cerium in order to make the La-rich Ce-poor compositions increasingly preferred, led to a glut of Ce-based raw materials at that time. In 1991, the La-rich Ce-poor portion of the raw material was in excess supply over demand.

Emission Control Catalysts. An application of growing importance for cerium is as one of the catalytically active components used to remove pollutants from vehicle (autoexhaust) emissions (36). The active form of cerium is the oxide that can be formed *in situ* by calcination of a soluble salt such as nitrate or by deposition of slurried oxide (see EXHAUST CONTROL, AUTOMOTIVE).

The most widely used exhaust control device consists of a ceramic monolith with a thin-walled open honeycomb structure. The accessible surface of this monolith system is increased by applying a separate coating, a wash coat, of a high surface area material such as gamma-alumina with the catalytically active species impregnated into this washcoat. The catalyst needs to oxidize hydrocarbons, convert CO to CO_2 , and reduce NO_x . The whole system forms a catalytic converter that, suitably encased, is placed between the engine and the muffler–silencer unit.

In addition to platinum and related metals, the principal active component in the multifunctional systems is cerium oxide. Each catalytic converter contains 50–100 g of finely divided ceria dispersed within the washcoat. Elucidation of the detailed behavior of cerium is difficult and complicated by the presence of other additives, eg, lanthanum oxide, that perform related functions. Ceria acts as a stabilizer for the high surface area alumina, as a promoter of the water gas shift reaction, as an oxygen storage component, and as an enhancer of the NO_x reduction capability of rhodium.

The tendency for high surface area gamma-alumina to sinter and lose that crucial area during high temperature operation is retarded by the intimate addition of several percent of cerium oxide. The mechanism is still under debate but may involve a surface LN –aluminate species on the alumina.

An oxygen storage component stores oxygen under lean operating conditions, ie, fuel-poor–air-rich, and releases it under fuel-rich, air-poor

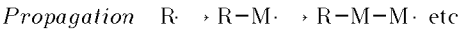
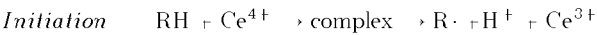
conditions to continue the oxidation of unburnt hydrocarbons and the removal of carbon monoxide even when there is insufficient gaseous oxygen. CeO₂ readily provides elemental oxygen by going nonstoichiometric to CeO_{2-x} in those air-poor portions of the exhaust cycle and then reoxidizing to CeO₂ during the air-rich period. The role of the cerium oxide however is more complex than just this oxygen storage capability. Overall ceria in autoexhaust catalysts provides better low temperature performance.

Combusion Additives. The ability of cerium oxide to act as an oxidizing agent underlies the potential use of various cerium derivatives as additives to aid combustion (see COMBUSTION TECHNOLOGY). Diesel exhaust often contains unburnt carbonaceous material as particulate matter, and in order to reduce particle emissions the exhaust can be passed through a ceramic trap, a closed honeycomb. In order to extend the lifetime of these traps and to reduce the temperature needed for regeneration, a cerium carboxylate, in particular cerium naphthenate, can be used as an additive to the fuel (37). The cerium compound, dissolved in the fuel at a concentration equivalent to around 25–50 ppm by weight of oxide, is transformed within the engine into CeO₂, which in turn is trapped in the so-called trap oxidizer. This finely divided oxide, thoroughly dispersed throughout the trap, produces conditions under which continuous regeneration effectively occurs; burn-off happens at a lower temperature because CeO₂ catalyzes the carbon combustion.

Sulfur Oxide Removal. In the refinery catalytic cracking process (FCC) sulfur-containing crude oil fractions can give rise to sulfur oxide in the gases emitted under the oxidizing conditions in the high temperature (750°C) regenerator unit. An additive to the actual FCC catalyst can capture this regenerator-SO_x as sulfate and later release, in the cracking, (reducing) region, a more easily trapped form of sulfur, H₂S. Several catalyst additives containing cerium and or lanthanides can act as the SO_x control agent by forming a stable sulfate that is reducible at the operating temperatures of the riser reactor.

Cerium oxide acts as a catalytic oxidizer in a spinel-based additive (38) that aids SO₂ to SO₃ conversion and promotes the required sulfate formation. Bastnasite itself is the most economical source of cerium and can be used directly at ~1% as the capture additive (39).

Polymerization Initiator. Some unsaturated monomers can be polymerized through the aid of free radicals generated, as transient intermediates, in the course of a redox reaction. The electron-transfer step during the redox process causes the scission of an intermediate to produce an active free radical. The ceric ion, Ce⁴⁺, is a strong one-electron oxidizing agent that can readily initiate the redox polymerization of, for example, vinyl monomers in aqueous media at near ambient temperatures (40). The reaction scheme is



where the monomer M can be methylmethacrylate, acrylamide, etc (see ACRYLAMIDE).

Cellulose and similar materials are polyhydric alcohols having hydroxyl groups that can react with ceric ions. The resulting macroradicals provide active sites for the polymerization of monomer with the special advantage that the radicals remain attached to the backbone polymer and hence copolymerization can occur without homopolymer being formed. Ceric ions can initiate graft polymerization of vinyl monomers onto wool, starch, cotton, and the like thereby modifying the properties of the natural polymer in order to, for example, improve mechanical strength.

Dehydrogenation, Ammoxidation, and Other Heterogeneous Catalysts. Cerium has minor uses in other commercial catalysts (41) where the element's role is probably related to Ce(III)–Ce(IV) chemistry. Styrene is made from ethylbenzene by an alkali-promoted iron oxide-based catalyst. The addition of a few percent of cerium oxide improves this catalyst's activity for styrene formation presumably because of a beneficial interaction between the Fe(II)–Fe(III) and Ce(III)–Ce(IV) redox couples. The ammoxidation of propylene to produce acrylonitrile is carried out over catalytically active complex molybdates. Cerium, a component of several patented compositions (42), functions as an oxygen and electron transfer through its redox couple.

Lubrication Additive. Cerium fluoride, CeF₃, can be used as an additive to lubricant formulations to improve extreme pressure and antiwear behavior (43). The white solid has a crystal structure that can be pictured as [CeF] layers separated by [F] atom sheets, a layer structure analogous to that of MoS₂, a material that CeF₃ resembles in properties.

Carbon Arcs. An electric arc struck between two rods of carbon can be a source of very intense light approximating sunlight in quality. The efficiency with which the input electrical energy is converted to the radiant visible energy can be enhanced by making the electrode rod with a core of lanthanide fluoride, (Ce,Ln)F₃. The function of the cerium and other lanthanides is to increase the light's intensity by the absorption of energy resulting in excitation of the Ln atoms to higher energy states. These excited atoms then emit light, falling back to their normal ground energy states. The atomic emission spectra of cerium and other lanthanides have many lines in the visible.

Paint Driers and Polymer Additives. Paints based on alkyd resins (qv) dry by the oxidation and cross-linking of unsaturated side chains. Metal catalysts are included in paint formulations to promote this drying. Cerium carboxylates, eg, the naphthenate, are used as through driers, ie, to promote drying in the body of the paint film rather than at the film's surface (44).

Silicones are oligomers and polymers, with good high temperature stability, based on the siloxane –O–Si–O–Si– backbone that itself is insensitive to oxidative scission, a degradation mechanism common to –C–C–C– backbone polymers. The oxidative stability, however, of the side chain groupings can remain a weak point for the molecule. Additives, in particular cerium derivatives (45), can improve properties. Metal soaps, such as the cerium octanoate, blended into the polymer can enable, for example, silicone fluids to be used at 250°C. Thermal degradation proceeds through free-radical reactions and the function of the cerium is, through the potential one-electron redox Ce(IV)–Ce(III) system, to mop up these radicals. Low levels of additive are effective because the behavior of cerium appears to be catalytic. Any Ce(III) formed is reoxidized back to the active Ce(IV) by the slow diffusion of oxygen air through the silicone.

Phosphor/Luminescence Applications.

Fluorescent Lighting Phosphors. Fluorescent lighting relies on phosphors to convert the efficient low pressury mercury-arc emission at 254 nm in the ultraviolet into energy emitted within the visible spectrum, 400 nm to 700 nm. Until the mid-1970s the phosphors of choice were halophosphates and others that produced an essentially continuous broad white-light spectrum. It was shown then that, for the visual perception of white, three line-emitting phosphors would suffice. Such a blend of three phosphors, with narrow line emissions centered at ~450, ~550, and ~610 nm, is not only more efficient in converting input electrical energy to output luminance but can also provide excellent color rendition. Cerium is an essential component in these new generation phosphors that have made possible the so-called tricolor lamps, essential for energy efficient and compact fluorescent lighting (46).

The role of cerium in these lighting phosphors is not as the emitting atom but rather as the sensitizer. The initial step in the lighting process is the efficient absorption of the 254 nm emission; Ce³⁺, with broad absorption bands in the uv, is very suitable. This absorbed energy is then transferred to the sublattice within the crystalline phosphor; eventually the activator ion is fed and emission results. Cerium, as a sensitizer ion, is compatible in crystal lattices with other lanthanide ions, such as Eu and Tb, the usual activator atoms.

The precise choice of compound for the phosphor depends on a complex interplay of symmetry, interatomic spacing, stability, etc in the crystal structure. The initial green emitting phosphor was the aluminate Ce_{0.7}Tb_{0.33}MgAl₁₁O₁₉. More recently the choice has been a (La_{0.4}Ce_{0.45}Tb_{0.15})PO₄ compound and in addition a borate, (Ce,Gd,Tb)MgB₅O₁₀, is also now used.

Another Ce-containing fluorescent lighting phosphor is Y₃Al₅O₁₂:Ce used in some blends to convert energy from the otherwise unwanted 435 nm mercury line from the blue into the yellow, lowering the color temperature of the light. This same garnet phosphor is also used in high pressure mercury discharge lamps for the same effect.

Cathode Ray Tube Phosphors. The cerium atom, upon excitation by energetic cathode ray electrons, produces a characteristic emission (luminescence) that is usually in the blue to ultraviolet region, the precise wavelength depending on the symmetry and nature of the ions immediately surrounding the Ce atom in the host lattice. The Ce³⁺ emission is highly efficient, is broadband in character, and corresponds to a 5d–4f transition. Because the transition is allowed the emitting energy level has a very short (~50 ns) lifetime and the luminescence decays very rapidly. This property underlies the use of some cerium-containing phosphors in specialized cathode-ray tube applications (47).

Beam-indexing display tubes require phosphors that emit ultraviolet when struck by an electron beam. The phosphor needs a high efficiency and an extremely fast decay time; the preferred material is cerium doped (~2 atomic %) yttrium diorthosilicate, Ce:Y₂Si₂O₇, having a peak emission at 380 nm. A flying-spot scanner images a transparent film and converts the image to an electronic signal with a very fast phosphor covering the whole visible spectrum. Two cerium-containing components, a garnet, Ce:Y₃Al₅O₁₂, and a silicate, Ce:Y₂SiO₅, the first emitting in the range 500–650 nm and the second over the range 370–500 nm, are combined to give the correct phosphor properties.

Cando-Luminescence, Gas Mantles. The role of a gas mantle is to produce visible radiation, in excess of the expected black-body thermal radiation, from an impinging gas flame. The closely woven fabric is impregnated with the nitrate solution that decomposes on heating to leave the oxide mantle adopting the fine structure of the textile yet having reasonable mechanical stability. The resulting oxide Ce_{0.01}Th_{0.99}O₂ has a broad emission band centered around 500 nm covering most of the visible; the trace of cerium moves the emission from the violet end into the visible and hence the emission becomes more pleasing to the eye. In addition it is probable that ceria is acting catalytically to ensure complete combustion.

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CERMETS.

See CARBIDES, CEMENTED CARBIDES; COMPOSITE MATERIALS, CERAMIC MATRIX; GLASSY METALS.

CESIUM AND CESIUM COMPOUNDS

Cesium [7440-46-2], Cs, is a member of the Group 1 alkali metals. It resembles potassium and rubidium in the metallic state, and the chemistry of cesium is more like that of these two elements than like that of the lighter alkali metals.

Cesium, first discovered by Bunsen and Kirchoff in 1860 while examining spring water, was the first element discovered spectroscopically (1). The name, comes from the Latin *caesius*, sky blue, and refers to the characteristic blue spectral lines of the element. Cesium salts were not successfully reduced to metal until 1881. Electrolysis of the molten chloride did not yield cesium metal under the same conditions that led to the reduction of the other alkali metal chlorides.

Cesium was first produced in the metallic state by electrolysis of a molten mixture of cesium and barium cyanides (2). Subsequently the more common thermochemical–reduction techniques were developed (3,4). There were essentially no industrial uses for cesium until 1926, when it was used for a few years as a getter and as an effective agent in reducing the electron work function on coated tungsten filaments in radio tubes. Development of photoelectric cells a few years later resulted in a small but steady consumption of cesium and other applications for cesium in photosensing elements followed.

Until the late 1970s cesium continued to be little more than a research element. Much of its limited production was for research into thermionic power conversion, magnetohydrodynamics (qv), and ion propulsion. Although the potential for these applications has not materialized, cesium chemical usage has increased significantly as catalysts in the chemical and petrochemical industries and in biotechnical engineering (see GENETIC ENGINEERING; NUCLEIC ACIDS).

Physical Properties

Pure cesium is a silvery white, soft, ductile metal. Surface alteration by minute traces of oxygen result in the metal taking on a golden hue. Of the stable alkali metals, ie, excluding francium, cesium has the lowest boiling and melting point, the highest vapor pressure, the highest density, and the lowest ionization potential. These properties and the large radius of the monovalent cesium ion have important consequences directly related to applications (5). Selected physical properties are given in Table 1.

Table 1. Physical Properties of Cesium

Property	Value
atomic number	55
atomic weight	132.905
melting point, °C	29
boiling point, °C	685
specific gravity, kg m ³	
solid at 17°C	1892
liquid at 40°C	1827
atomic radius, ^a nm	0.274
ionic radius, ^b nm	0.165
viscosity at mp, mPas (cP)	0.686
surface tension at mp, mN m	39.4
heat of fusion, Δ <i>H</i> _{fus} , kJ mol ^c	2.13
heat of vaporization, Δ <i>H</i> _{vap} , at 0.1 MPa, J mol ^{c,d}	65.9
specific heat, J g°C ^c	
solid at 20°C	0.217
liquid at bp	0.239
vapor at bp	0.156
thermal conductivity, W (m°C)	
liquid at mp	18.4
vapor at bp	4.6 × 10 ⁻³
ionization potential, eV	3.893
work function, eV	1.91
standard electrode potential, V	2.923
electrical conductivity, (Ωm) ⁻¹	
solid at mp	4.9 × 10 ⁶
vapor at 1250°C	2.0 × 10 ⁴
Moh's hardness	0.2
Brinell hardness, kg mm ²	0.015

^a The metal is 12 coordinate
^b The ion is usually 6 coordinate
^c To convert J to cal, divide by 4.184.
^d To convert MPa to psi, multiply by 145.

Chemical Properties

The ionization potential of the alkali metals decreases with increasing atomic number; consequently cesium is generally far more reactive than the lower members of the alkali metal group. When cesium is exposed to air, the metal ignites spontaneously and burns vigorously producing a reddish violet flame to form a mixture of cesium oxides. Similarly cesium reacts vigorously with water to form cesium hydroxide, the strongest base known, as well as hydrogen; together with air and water a hydrogen explosion usually occurs as the burning cesium readily ignites the liberated hydrogen gas. Cesium, the most active of the alkali metals toward oxygen and the halogens, is the least reactive toward nitrogen, carbon, and hydrogen.

Cesium salts are, in general, chemically similar to other alkali metal salts. The solubility of alkali-metal salts of simple anions generally increases with the atomic weight of the alkali ion; in contrast the solubility of the alkali-metal salts of complex anions generally decreases with increasing atomic weight. The salts of cesium and simple anions are usually hygroscopic as well as very soluble, but the sparingly soluble salts of cesium and complex anions are seldom hydrated and are usually not hygroscopic.

Cesium forms simple alkyl and aryl compounds that are similar to those of the other alkali metals (6). They are colorless, solid, amorphous, nonvolatile, and insoluble, except by decomposition, in most solvents except diethylzinc. As a result of exceptional reactivity, cesium aryls should be effective in alkylations wherever other alkaline alkyls or Grignard reagents have failed (see GRIGNARD REACTIONS). Cesium reacts with hydrocarbons in which the activity of a C–H link is increased by attachment to the carbon atom of doubly linked or aromatic radicals. A brown, solid addition product is formed when cesium reacts with ethylene, and a very reactive dark red powder, triphenylmethylcesium [76-83-5], (C H₅)₃CCs, is formed by the reaction of cesium amalgam and a solution of triphenylmethyl chloride in anhydrous ether.

Occurrence

Cesium is the rarest of the naturally occurring alkali metals, ranking 40th in elemental prevalence. Nevertheless, it is widely distributed in the earth's crust at very low concentrations. Granites contain an average of about 1 ppm (7), sedimentary rocks about 4 ppm (8), and seawater about 0.2 ppm (9). Higher concentrations are found in lepidolite [1317-64-2], a lithium mica containing approximately 0.5% Cs₂O but reaching 1.9% on rare occasions (10), in carnallite [1318-27-0], KMgCl₃ ·6H₂O, a double salt of potassium and magnesium chlorides containing 10–40 ppm Cs₂O; in the rare mixed cesium–antimony–tantalum oxide cestibtantite (11); as well as in muscovite, beryl, spodumene, potassium feldspars, leucite, petalite, and related minerals. Both lepidolite and carnallite have yielded commercial quantities of cesium (12) and a process for its recovery from muscovite micas has been developed (13).

By far the most important commercial cesium source is pollucite [1308-53-8], ideally Cs₂O ·Al₂O₃ ·4SiO₂. The theoretical cesium content of pure pollucite is 45 wt % Cs₂O; however natural pollucite usually contains 5–32% Cs₂O because of other minerals intimately associated with the pollucite. Additionally, the Cs is often replaced in the crystal lattice by varying amounts of Rb, K, or Na plus H₂O. Natural pollucite can be regarded as an intermediate mineral in the isomorphous series analcime [1318-10-1], Na₂O ·Al₂O₃ ·4SiO₂ ·2H₂O, and theoretical pollucite (14). Pollucite is a clear to milky greyish mineral with uneven fracture, similar to quartz but from which it can generally be distinguished by the ubiquitous veinlets of alteration products that occur in the pollucite (14). Alternatively, a qualitative field test that produces a bright red reaction stain (15) can be used to ascertain its presence.

Economic concentrations of pollucite usually occur in highly zoned complex pegmatites, associated with lepidolite, petalite, and spodumene. The Bernic Lake orebody of Tantalum Mining Corp. of Canada Ltd. (Tanco) in southeastern Manitoba, Canada, is the world's largest cesium source containing approximately two-thirds of the known ore. The pollucite occurs as essentially monomineralic zones within a flat lying pegmatite having a spatial extent of some 3 km². The main zones contain over 400,000 tons of pollucite grading approximately 24% Cs₂O with another zone of 100,000 tons of 5% ore (16). Tanco's production accounts for about two-thirds of the world's requirements. Other significant ore deposits are the Bikita pegmatite in Zimbabwe, and in the Karibib desert of Namibia (17). Other, smaller concentrations occur in Brazil, where some production takes place, as well as Scandinavia, Czechoslovakia, Afghanistan, and the United States. Some ore was mined from a deposit in Maine between World Wars I and II, but there has been no U.S. production for several decades. Russia has some low-grade resources, but the evidence points to them not being exploited, presumably because of low grade. The known high-grade reserves of pollucite are sufficient to supply a steady demand for well over a century, and since 1960, cesium has essentially been produced from pollucite.

Processing of Pollucite

Pollucite preparation consists simply of mining the ore, crushing it to required size, followed in some instances by hand picking. No other concentration is required. Although flotation processes for the concentration of low-grade ores have been developed in both the United States and Russia (18), these have commercially lagged because of the availability of high-grade ores (19). Chemetall GmbH, Frankfurt, Germany, a Division of Metallgesellschaft AG, is the predominant processor worldwide; the only significant U.S. producer is Cabot Corp., Electronic Materials and Refractory Metals Division, at their Revere, Pennsylvania plant. Other, smaller, established producers include Daiichi Kigenso K.K. in Japan and BDH in the UK. There are other newer, production facilities in Denmark and Japan. Russia produces, at least partially, from imported sources of pollucite.

There are three basic methods of converting pollucite to cesium metal or compounds: direct reduction with metals; decomposition with bases; and acid digestion. In each case grinding of the ore to 75 μm precedes conversion.

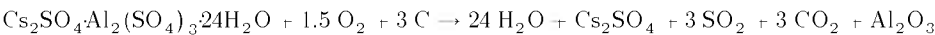
Direct Reduction with Metals. Pollucite can be directly reduced by heating the ore in the presence of calcium to 950°C in a vacuum (20), or in the presence of either sodium or potassium to 750°C in an inert atmosphere (21). Extraction is not complete. Excessive amounts of the reducing metal is required and the resultant cesium metal is impure except when extensive distillation purification is carried out. Engineering difficulties in this process are significant, hence, this method is not commercially used.

Decomposition with Bases. Alkaline decomposition of pollucite can be carried out by roasting pollucite with either a calcium carbonate–calcium chloride mix at 800–900°C or a sodium carbonate–sodium chloride mix at 600–800°C followed by a water leach of the roasted mass, to give an impure cesium chloride solution that is separated from the gangue by filtration (22). The solution can then be converted to cesium alum [7784-17-0], Cs₂SO₄ ·Al₂(SO₄)₃ ·24H₂O. Extraction of cesium from the pollucite is almost complete. Solvent extraction of cesium carbonate from the cesium chloride solution using a phenol in kerosene has also been developed (23).

Acid Digestion. Acid digestion of pollucite is the primary commercial process for cesium production. Hydrofluoric, hydrobromic, hydrochloric, and sulfuric acids can be used. Hydrofluoric acid has been used in Germany (24); it gives the most complete cesium recovery, but the inherent difficulties with its use eliminate any current advantage. Likewise, the proposed hydrobromic acid process (25), which converts pollucite to the bromide that is precipitated using isopropyl alcohol from which the cesium is removed by liquid bromine, is not in use in part because of the engineering problems associated with the hot acids.

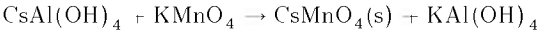
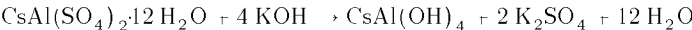
Hydrochloric acid digestion takes place at elevated temperatures and produces a solution of the mixed chlorides of cesium, aluminum, and other alkali metals separated from the siliceous residue by filtration. The impure cesium chloride can be purified as cesium chloride double salts such as cesium antimony chloride [14590-08-0], 4CsCl SbCl₃, cesium iodine chloride [15605-42-2], Cs₂Cl₂I, or cesium hexachloroerate [19153-44-7], Cs₃[CeCl₆] (26). Such salts are recrystallized and the purified double salts decomposed to cesium chloride by hydrolysis, or precipitated with hydrogen sulfide. Alternatively, solvent extraction of cesium chloride direct from the hydrochloric acid leach liquor can be used.

Sulfuric acid digestion has been investigated by several laboratories, including the Canadian Mines Branch (CANMET), Ottawa, Canada (27). Pollucite is digested at 110°C, close to the boiling point of 35–40% sulfuric acid, followed by a hot water wash and vacuum filtration. Cesium alum is crystallized from the leach filtrate by stage cooling to 50°C and then to 20°C, and roasted in the presence of 4% carbon



The residue is leached to give cesium sulfate solution, which can be converted to cesium chloride by ion exchange on Dowex 50 resin and elution with 10% HCl, treatment using ammonia or lime, to precipitate the aluminum, or by solvent extraction, followed by purification at neutral pH using hydrogen peroxide or ammonia.

In one process developed by Carus Corp., Illinois, pollucite is digested with sulfuric acid to cesium alum that is dissolved in an aqueous hydroxide solution to form cesium alum hydroxide and potassium sulfate, from which cesium permanganate is directly precipitated by addition of potassium permanganate (28).



Alternatively, permanganate can be added to the cesium chloride resulting from hydrochloric acid digestion, after removal of excess iron and alumina by precipitation as hydroxides, followed by centrifugation and filtration (29) to pure cesium permanganate. The resultant cesium permanganate can be converted to the carbonate or chloride by reduction using an agent such as methanol.

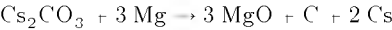
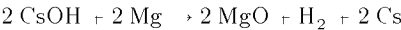
Production of Cesium Metal

The primary producer of cesium metal in the United States is Cabot Corp.

Thermochemical Methods. Cesium halides can readily be reduced using calcium or barium, but not magnesium. Purified cesium chloride and calcium in roughly equal proportions are heated together to 700–800°C under a vacuum or in an atmosphere of an inert gas such as argon or helium, and 90–95% of the cesium is distilled as metal (30), although lower temperatures (300–400°C) and higher vacuum achieve the same result but with higher purity (31).

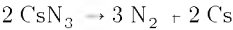


Magnesium is used to obtain cesium metal from cesium hydroxide [21351-79-1], Cs(OH), cesium carbonate [534-17-8], Cs₂CO₃, or cesium aluminate [20281-00-9], Cs₂O·Al₂O₃, according to the equations (31)



Vacuum redistillation at low temperature is used for final purification of the cesium metal, if required.

Thermal Decomposition. Cesium azide [22750-57-8], CsN₃, which is prepared by reacting aqueous solutions of cesium sulfate and barium azide, melts at 326°C and decomposes at 390°C to cesium metal (32):



Electrolytic Reduction. The extreme reactivity and relatively high volatility of cesium metal combine to make conventional fused-salt electrolysis of cesium salts impractical for the direct production of cesium metal, although it can be used as one stage in metal production. For example, electrolysis of fused cesium chloride using a molten lead cathode at 700°C results in a cesium–lead alloy containing about 8.5% Cs, from which cesium metal can be distilled at 600–700°C under vacuum (27). Alternatively, electrolysis of concentrated aqueous solutions using a mercury cathode can be followed by distillation of the amalgam resulting in cesium metal (33).

Cesium Alloys

Eutectics melting at about –30, –47, and –40°C are formed in the binary systems, cesium–sodium at about 9% sodium, cesium–potassium at about 25% potassium, and cesium–rubidium at about 14% rubidium (34). A ternary eutectic with a melting point of about –72°C has the composition 73% cesium, 24% potassium, and 3% sodium. Cesium and lithium are essentially completely immiscible in all proportions.

Cesium does not alloy with or attack cobalt, iron, molybdenum, nickel, platinum, tantalum, or tungsten at temperatures up to 650°C (35).

Cesium Compounds

Cesium compounds are manufactured and distributed by a comparatively large number of companies, considering the size of the total cesium market. Those companies that process pollucite produce their own range of products, some of which are then reprocessed and refined by other, smaller, specialty companies, many of which are located in the United States.

Carbonates. Cesium carbonate [534-17-8], Cs₂CO₃, mol wt 325.82, specific gravity 4072 kg m^{–3}, has theoretical cesium content of 81.58%. It is a colorless, very hygroscopic, crystalline solid, which is stable up to its melting point of 610°C at which temperature it decomposes. The carbonate is prepared from the hydroxide by the addition of carbon dioxide, but it can also be prepared by decomposing the nitrate with excess oxalic acid to form the oxalate and igniting and decomposing the cesium oxalate to the carbonate.

Cesium hydrogen carbonate [15519-28-5], CsHCO₃, mol wt 193.92, theoretical cesium content 68.54%, is a colorless, slightly hygroscopic, crystalline solid having a specific gravity of ca 1400 kg m^{–3}, which decomposes at 175°C. It has a solubility of 2.1 kg L.

Cesium Chromate. Cesium chromate [13454-78-9], Cs₂CrO₄, has a mol wt 381.80, and a theoretical cesium content of 69.62 wt %.

Cesium Halides. Cesium bromide, [7787-69-1], CsBr, mol wt 212.82, theoretical cesium content 62.45%, is a colorless crystalline solid, having a melting point of 636°C, a specific gravity of 4433 kg m^{–3}, and a solubility of 1.23 kg L of water at 25°C. It is usually prepared by neutralizing the carbonate or hydroxide with HBr, but it is also the primary product of the Dow process (25) for pollucite processing.

Cesium chloride, [7647-17-8], CsCl, mol wt 168.36, theoretical cesium content 78.9%, has a melting point of 646°C, a boiling point 1290°C, and a specific gravity of 3983 kg m^{–3}. Cesium chloride is a primary product of pollucite processing using hydrochloric acid digestion, and it is usually purified by precipitation as a complex double salt, which is then decomposed by hydrolysis or sulfide precipitation, leaving purified cesium chloride in solution. It crystallizes readily from water in well-defined, colorless, cubic crystals; its solubility is 2.7 kg L of water at 100°C, 1.86 kg L at 20°C, and 1.62 kg L at 0°C. It can be formed by neutralization of the carbonate or hydroxide with hydrochloric acid.

Cesium perchlorate [13454-84-7], CsClO₄, mol wt 232.35 and theoretical cesium content 57.2%, is a crystalline powder that decomposes at 250°C

Cesium fluoride [13400-13-0], CsF, mol wt 151.90, theoretical cesium content 87.49%, has a melting point of 682–703°C and a boiling point of 1253°C. Cesium fluoride is an extremely hygroscopic, colorless, crystalline solid; it has a solubility of 3.665 kg L of water at 18°C. Cesium fluoride is made by exactly neutralizing cesium hydroxide with hydrofluoric acid and evaporating the resultant solution to dryness at 400°C. Excess HF results in a bifluoride salt that does not decompose at 400°C, and carbonate in the starting material gives an alkaline product.

Cesium iodide [7789-17-5], CsI, mol wt 259.81, theoretical cesium content 51.2%, has a melting point of 621°C and a specific gravity of 4510 kg m^{–3}. It is colorless, crystalline, hygroscopic, and has a solubility of 0.74 kg L of water at 20°C, and 1.6 kg L at 61°C. It is formed by the neutralization of the hydroxide or carbonate using hydriodic acid.

Cesium Hydroxide. Cesium hydroxide [21351-79-1], CsOH, mol wt 149.91, theoretical cesium content 88.66%, is a colorless, crystalline, hygroscopic, anhydrous, lumpy solid, having a melting point of 272°C and a specific gravity of 3680 kg m⁻³. It has a solubility of about 4 kg L of water at 15°C and is sold both in the solid form and as a 50% solution. It is the strongest base known, and hot, concentrated cesium hydroxide rapidly attacks nickel and silver, which are often used as container materials for less reactive hydroxides. Cesium hydroxide solutions can be dehydrated in platinum at 180°C to give the monohydrate, and further dehydration at 400°C, in a vacuum, results in the anhydrous solid being formed. Carbon dioxide (qv) is absorbed rapidly from the air by both the solid and aqueous solutions of cesium hydroxide. Reaction of the solid hydroxide and carbon monoxide at atmospheric pressure and elevated temperature results in the formation of cesium formate [3495-36-1], CsHCO₂, cesium oxalate [18365-41-8], Cs₂C₂O₄, and the carbonate.

Cesium hydroxide monohydrate [35103-79-8], CsOH ·H₂O, mol wt 167.93, theoretical cesium content 79.14 wt %, is a colorless, hygroscopic, crystalline powder, having a melting point of 205–208°C and a specific gravity of 3500 kg m⁻³. It is highly soluble, 8.6 kg L of water at 15°C; similar to the anhydrous hydroxide, it is an extremely strong base.

Cesium Nitrate. Cesium nitrate [7789-18-6], CsNO₃, mol wt 194.91, theoretical cesium content 68.19 wt %, crystallizes from solution in well-defined, glittering, colorless, hexagonal prisms. It has a melting point of 414°C, a specific gravity of 3685 kg m⁻³, and a solubility of 0.09 kg L of water at 0°C, and 1.97 kg L at 100°C. Cesium nitrate is prepared from the chloride by heating with excess nitric acid until a negative test for chlorides is obtained; the reverse conversion to chloride using excess hydrochloric acid is also possible. Cesium nitrate is an ideal salt for obtaining cesium free from other alkalies, as fractional crystallization from water effectively eliminates traces of lithium, sodium, potassium, and rubidium.

Cesium Oxides. Cesium forms a series of oxides, including cesium monoxide [20281-00-9], Cs₂O, mol wt 281.81, theoretical cesium content 94.32 wt %; the suboxides: cesium heptaoxide [12433-62-4], CsO₇, tetracesium oxide [12433-60-2], Cs₄O, heptacesium dioxide [12433-63-5], Cs₇O₂, and tricesium oxide [12433-59-9], Cs₃O; cesium peroxide [12053-70-2], Cs₂O₂; and cesium superoxide [12018-61-0], CsO₂. The suboxides are formed by incomplete oxidation of cesium metal or by treating cesium monoxide with cesium metal. Cesium monoxide can be formed by direct combination of the elements or by thermal decomposition of the suboxides in the form of polycrystalline laminated plates, which are lemon yellow at 80°C, orange-yellow at room temperature, and cherry red above 180°C. The crystal structures of both Cs₂O and Cs₃O have been determined by single-crystal x-ray studies (36).

Partial oxidation of cesium metal changes its color from silver-white to golden yellow; further oxidation using dry oxygen gives a black reaction product which, in the presence of oxygen at 330°C, changes to the bright yellow superoxide, CsO₂. Thermal decomposition of this product at 280–360°C yields the peroxide, without the formation of intermediate sesquioxide; further decomposition results in the monoxide (37).

Cesium Permanganate. Cesium permanganate [13456-28-5], CsMnO₄, mol wt 251.84, theoretical cesium content 52.77 wt %, has a specific gravity of 3597 kg m⁻³, decomposes at 320°C, and is relatively insoluble at about 1 g L of water. It is prepared in the Carus process by precipitation through the reaction of hydrated cesium alum with potassium permanganate (28). It can be reduced to cesium chloride or cesium carbonate using a reducing agent such as methanol.

Cesium Sulfates. Cesium sulfate [10294-54-9], Cs₂SO₄, mol wt 361.87, theoretical cesium content 73.46 wt %, forms colorless, rhombic, or hexagonal crystals and has a melting point of 1010°C and a specific gravity of 4243 kg m⁻³. It can be obtained by adding a hot solution of barium hydroxide to a boiling solution of cesium alum until all the aluminum is precipitated. This equivalence point is well indicated by spot-testing for alkalinity using bromthymol blue, which has pH 7.6. Filtration yields a filtrate barren of aluminum hydroxide and barium sulfate, and the cesium sulfate is then obtained by concentration and recrystallization from water.

Cesium aluminum sulfate [7784-17-0] (cesium alum) Cs₂SO₄ ·Al₂(SO₄)₃ ·24H₂O, mol wt 1136.39, theoretical cesium content 23.39 wt %, has a melting point of 117°C and a specific gravity of 1970 kg m⁻³. It is the least soluble of the alkali alums, having a solubility of about 0.32 kg L of water at 100°C but only 0.015 kg L at 50°C. It therefore crystallizes first from aqueous mixed solutions of the alkali alums, as colorless, octahedral crystals and can readily be separated completely from lithium, sodium, and potassium alums by fractional distillation; the relative solubility of rubidium alum is such, however, that multiple-stage fractional crystallization is required to effect a separation. Cesium alum is the digestion product of pollucite in sulfuric acid and is one of the starting points for the production of cesium compounds.

Other Cesium Compounds. Cesium acetate [3396-11-0], CsOOCCH₃, mol wt 191.95, theoretical cesium content 69.24 wt %; cesium trifluoroacetate, CF₃COOCs, mol wt 245.93, theoretical cesium content 54.04 wt %; cesium–precious metal compounds such as cesium dicarbonyltetrachlororuthenium, [22594-81-6] Cs₂RuCl₄(CO)₂, mol wt 564.71, ruthenium content of 17.9 wt %, a yellow crystalline powder; and cesium tetrachlorogold [13682-60-5], CsAuCl₄, mol wt 471.7, gold content of 41.8 wt % a yellow powder; are all known.

Economic Aspects

The price of pollucite, 24% grade, has been in the range of \$600 to \$1000 per metric ton and the price of cesium metal in the range of \$600 to \$700 per kilogram since the early 1980s. The price of cesium compounds varies widely depending on the compound and both quantity and quality. Technical-grade compounds were priced in the range \$75–140 kg (38); the price of the cesium–precious metal compounds more than \$400 g. Many of the available cesium compounds are packaged in small quantities ranging from 1 to 100 g, indicating consumption levels.

Most current applications require relatively small quantities of cesium, and hence annual world production of cesium metal and compounds is estimated to be on the order of 250 t of cesium chloride equivalents.

Handling, Storage, Transportation, and Occupational Health

Because of the high reactivity of cesium metal, special precautions are required for its storage, transportation, and use. Small quantities are usually contained in evacuated glass ampuls, larger quantities in stainless steel containers which are themselves contained in an outer packing, ensuring that the metal is kept from moisture or air. Most cesium compounds are hygroscopic, especially the halides, and must therefore be stored dry. Other precautions that must be taken depend on the anion. Most products are sold in polyethylene bottles inside of clamping ring steel drums.

The cesium ion is more toxic than the sodium ion but less toxic than the potassium, lithium, or rubidium ion. No TLV is stated for cesium or cesium chloride; the TLV for cesium hydroxide is 2 mg m⁻³. The oral LD₅₀ of cesium chloride for mice is 2300 mg kg, and for cesium fluoride is 400–700 mg kg (39).

The toxicology, occupational health hazards, and transportation regulations of cesium compounds result from the anion rather than the cesium cation. Producers and distributors provide an MSDS as well as detailed shipping requirements for each product.

Standards and Analytical Procedures

The determination of cesium in minerals can be accomplished by x-ray fluorescence spectrometry or for low ranges associated with geochemical exploration, by atomic absorption, using comparative standards. For low levels of cesium in medical research, the proton induced x-ray emission technique has been developed (40).

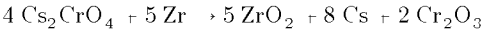
Cesium metal and cesium compounds are produced and marketed in a variety of grades, eg, from 99% for technical grades to as high as 99.999% for ultrapure compounds.

Analysis and purities of the metal or compounds are determined by difference, subtracting the sum of the analyzed levels of all impurities from 100%. Analysis of impurity levels is carried out by the most appropriate technique, which may include spectroscopy, atomic absorption, and photometry.

Uses

The number of commercial uses of both cesium metal and its compounds has grown significantly since the early 1980s.

Electronic Applications. Electronic applications make up a significant sector of the cesium market. The main applications are in vacuum tubes, photoemissive devices, and scintillation counters (see ELECTRONIC MATERIALS).
Vacuum Tubes. In the manufacture of vacuum tubes for use in polarized ion sources, vaporized cesium is used as a getter for residual gaseous impurities in the tube and as a coating to reduce the work function of the tungsten filaments or cathodes of the tube. The cesium vapor is generated by firing, at about 850°C within the sealed and evacuated tube, a cesium chromate pellet and zirconium (12) (see VACUUM TECHNOLOGY).



Photoemissive Devices. The development of the silver–oxygen–cesium photoemitter, which converts photons into free electrons, resulted in commercial exploitation of photoemissive devices; the first important use was the reproduction of sound from film, followed by such devices as the photomultiplier, iconoscope, image orthicon, and optical character recognition devices (41) (see IMAGING TECHNOLOGY; PHOTODETECTORS). The Ag–O–Cs photoemitter has relatively low sensitivity, and most photoemitters are constructed using intermetallic compounds such as antimony tricesium [12018-68-7], SbCs₃, and the bialkali K–Cs–Sb, rather than alloys. In the photomultiplier tube, cesium is used both in the photocathode and also as a secondary emission material in the dynode. Photomultipliers are used in a wide range of equipment, including pollution and radiation monitoring equipment; scientific, military, and medical equipment; and gamma-ray cameras.

Scintillation Counters. Cesium iodide and cesium fluoride are used in scintillation counters, which convert energy from ionizing radiation into pulses of visible light. Such units have special application in the fields of medical diagnostics, oil and mineral exploration, analysis, and space, military, and nuclear physics research (42). Thallium activated cesium iodide monocrystals have been incorporated in a synchrotron for detecting high energy gamma rays (43). Cesium iodide and cesium bromide are used for the preparation of lenses, prisms, and cuvettes for use in infrared spectrometers, especially in the 500–550 nm range (see INFRARED AND RAMAN SPECTROSCOPY).

Other. Alkali chlorochromate compounds, including cesium chlorochromate, CsCrCl₄, are ferromagnetic substances being studied for potential application in optically-read computer memory devices. Cesium has also been used in vapor glow lamps (44), vapor rectifiers, and high energy lasers (qv) (45).

Biotechnology and Medical Applications. Cesium chloride, and to a lesser extent the other halides, cesium trifluoroacetate and cesium sulfate, are used in the purification of nucleic acids (qv), ie, RNA and DNA, viruses, and other macromolecules (46). Molecules are separated according to density after being subjected to a centrifugal density gradient. In medicine, cesium salts have been considered both as an antishock reagent following the administration of arsenical drugs, though a contraindication is the disturbance to heart rhythm (47), and for the treatment of epilepsy.

The isotope ¹³⁴Cs, *t*_{1/2} = 2.05 yr, emits a beta particle and is useful in radioautography (48). Research into the use of the stable ¹³³Cs isotope and the positron-emitter ¹³²Cs, *t*_{1/2} = 6.47 d, as well as ¹³¹Cs, *t*_{1/2} = 9.7 d, for cancer treatment has been carried out (49), although these processes have not yet been commercialized.

Chemical Applications. Cesium metal is used in carbon dioxide purification as an adsorbent of impurities; in ferrous and nonferrous metallurgy (qv) it can be used as a scavenger of gases and other impurities.

The performance of many metal-ion catalysts can be enhanced by doping with cesium compounds. This is a result both of the low ionization potential of cesium and its ability to stabilize high oxidation states of transition-metal oxo anions (50). Catalyst doping is one of the principal commercial uses of cesium. Cesium is a more powerful oxidant than potassium, which it can replace. The amount of replacement is often a matter of economic benefit. Cesium-doped catalysts are used for the production of styrene monomer from ethyl benzene at metal oxide contacts or from toluene and methanol as Cs-exchanged zeolites; ethylene oxide; ammonoxidation, acrolein (methacrolein); acrylic acid (methacrylic acid); methyl methacrylate monomer; methanol; phthalic anhydride; anthraquinone; various olefins; chlorinations; in low pressure ammonia synthesis; and in the conversion of SO₂ to SO₃ in sulfuric acid production.

A growing use of cesium compounds is in the field of organic synthesis, replacing sodium or potassium salts. Various cesium compounds are highly soluble in polar solvents. These compounds do not decompose as do many organic compounds, thus avoiding undesirable by-product formation. Additionally, the cesium component can be recovered and recycled. The use of cesium fluoride in esterifications is typical, eg, the synthesis of phenacyl esters (51); in the production of trialkyl phosphates, ie, a plasticiser (52); in polymerizations; and in the preparation of organofluorine compounds, such as ring fluorinated aromatics, by halogen exchange. In this latter case, it can be used either alone, as a catalyst to accelerate KF reactions, or in combination with calcium fluoride as a support reagent (53). Cesium carbonate can be used in intramolecular cyclizations; for example, cyclic oligoethers can be prepared utilizing the template effect of the cesium cation (54). Cesium hydroxide can be used for the synthesis of insoluble fatty acid esters and polyesters (52).

Molten (177–343°C) cesium hydroxide can be used in desulfurizing heavy oils. The hydroxide may be recycled by steam hydrolysis (55).

Energy Related Applications. Much research, with regard to the use of cesium in energy related processes, has resulted in little commercial application. The heightened awareness of the environmental degradation caused by fossil fuel power stations has resulted in increased research both into efficiency improvements for existing plants and into alternative power generation (qv) methods.

Cesium is ideally suited for use in magnetohydrodynamic (MHD) power generation. The metal can be used as the plasma seeding agent in closed-cycle MHD generators using high temperature nuclear reactors (qv) as the primary heat source. However, open-cycle MHD offers considerable potential for increasing the efficiency of fossil fuel fired power plants from 30–35% to 45–50%. Hot combustion gases are seeded using cesium oxide or cesium carbonate, potassium carbonate, or a mixture to form a highly conductive plasma that is accelerated through a magnetic field channel, ideally a superconducting magnet, and an electric current is generated at right angles to both the flow of plasma and the magnetic field. The off-gases thereafter pass to a conventional power generator. One of the significant potential side benefits of this process is the scrubbing of sulfur from the off-gases by the seeding material. Potassium carbonate is considerably cheaper but also much less effective than the cesium compounds; the use of a mixture of the salts has been proposed to be the best choice (56) (see PLASMA TECHNOLOGY).

MHD generated considerable interest in the 1960s and 1970s and by 1971, a 20 MW unit had been constructed in Russia. By 1986 a commercial-scale 500 MW plant was built at Ryazan. Interest elsewhere waned, but since the mid-1980s interest in the United States has again increased, resulting in plans to build pilot-plant versions (57).

One alternative method of generating electricity directly from a heat source is by the use of a cesium vapor thermionic convertor, which uses cesium to neutralize the space charge above a hot cathode that is emitting electrons toward a cooler anode. A nuclear reactor is required as the heat source because temperatures of about 1900°C are necessary (58). Cesium has also been considered as a working fluid for high temperature Rankine-cycle, turboelectric generators (59). Cesium oxide has been mentioned as a coating in solar photovoltaic cells (qv) (see SOLAR ENERGY), and cesium hydroxide has been considered as a partial replacement of sodium or potassium hydroxide in alkaline storage batteries (qv) especially for use at low temperatures (60), although lithium is now preferred.

Ion engines are used in satellites for orientation control. Cesium is vaporized in a vacuum and ionized as it passes through a heated porous tungsten disk, the ions are accelerated by an electric field to about 135 km/s and are neutralized by the injection of electrons and exhausted from the thruster. However, mercury, xenon, and argon-based ion engines are preferred.

Other Applications. The refractive index of silicate or borosilicate glass can be modified by the addition of cesium oxide, introduced as cesium nitrate or carbonate. Glass surfaces can be made resistant to corrosion or breakage by surface ion exchange with cesium compound melts or solutions. This process can also be used for the production of optical wave guides (61).

Cesium metal is used for time standards based on the natural vibration of the ¹³³Cs atom, which oscillates 9,192,631,770 times per second, and in high precision oscillators to synchronize fiber optic telecommunication.

It has been suggested that cesium may be useful in the fixation of radioactive waste in a cesium-based glass and in detoxification procedures for fugitive ¹³⁷Cs emissions, such as at Chernobyl, Ukraine.

Cesium Isotopes

Naturally occurring cesium and cesium minerals consist only of the stable isotope ¹³³Cs. The radioactive cesium isotopes such as ¹³⁷Cs are generated in fuel rods in nuclear power plants (38).

Cesium isotopes can be recovered from fission products by digestion in nitric acid, and after filtration of waste the radioactive cesium phosphotungstate is precipitated using phosphotungstic acid. This technique can be used to prepare radioactive cesium metal or compounds. Various processes for removal of ¹³⁷Cs isotopes from radioactive waste have been developed including solvent extraction using macrocyclic polyethers (62) or crown ethers (63) and coprecipitation with sodium tetraphenylboron (64).

The radioactive isotope ¹³⁷Cs is important commercially in process control instruments and for sewage sludge sterilization. The isotope has a long half-life (*t*_{1/2} = 30 yr); however, it must be well-shielded because of the high biological hazard.

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CHARCOAL.

See WOOD.

CHELATING AGENTS

A chelating agent, or chelant, contains two or more electron donor atoms that can form coordinate bonds to a single metal atom. After the first such coordinate bond, each successive donor atom that binds creates a ring containing the metal atom. This cyclic structure is called a chelation complex or chelate, the name deriving from the Greek word chela for the great claw of the lobster (1).

Chelation is an equilibrium system involving the chelant, the metal, and the chelate. Equilibrium constants of chelation are usually orders of magnitude greater than are those involving the complexation of metal atoms by molecules having only one donor atom.

Chelating agents may be used to control metal ion concentrations. Chelation complexes usually have properties that are markedly different from both the free metal ion and the chelating agent. Consequently, chelating agents provide a means of manipulating metal ions through the reduction of undesirable effects by sequestration or through creating desirable effects such as in metal buffering, corrosion inhibition, solubilization, and cancer therapy.

Chelates and chelation reactions are abundant in nature, ranging from delicately balanced life processes depending on traces of metal ions to extremely stable metal chelates in crude petroleum. Examples of biochemical processes involving chelates include photosynthesis, oxygen transport by blood, certain enzyme reactions, ion transport through membranes, and muscle contraction. Technological applications include scale removal from steam boilers, water softening, ore leaching, textile processing, food preservation, treatment of lead poisoning, chemical analysis, tissue specific medical procedures, and micronutrient fertilization of agricultural crops.

Structure and Terminology

The structural essentials of a chelate are coordinate bonds between a metal atom or a stable oxo cation, M, which serves as an electron acceptor, and two or more atoms in the molecule of the chelating agent, or ligand, L, which serve as the electron donors. A chelating agent may be bidentate, tridentate, tetradentate, and so on, according to whether it contains two, three, four, or more donor atoms capable of simultaneously complexing with the metal atom. Examples are shown in Figure 1. Molecules having only one donor atom, such as water and dimethylamine, are monodentates and form coordination complexes but not chelates. The principal donor atoms in practical use are N, O, and S, but P, As, and Se also form chelates. Metals are characterized by coordination numbers which correspond to the number of donor atoms bound to the central metal atom in a particular compound. The most common coordination numbers are four and six. Some metals have more than one coordination number, depending on the valence state. The term coordination number also refers, albeit less commonly, to the maximum number of donor atoms to which the metal atom can coordinate.

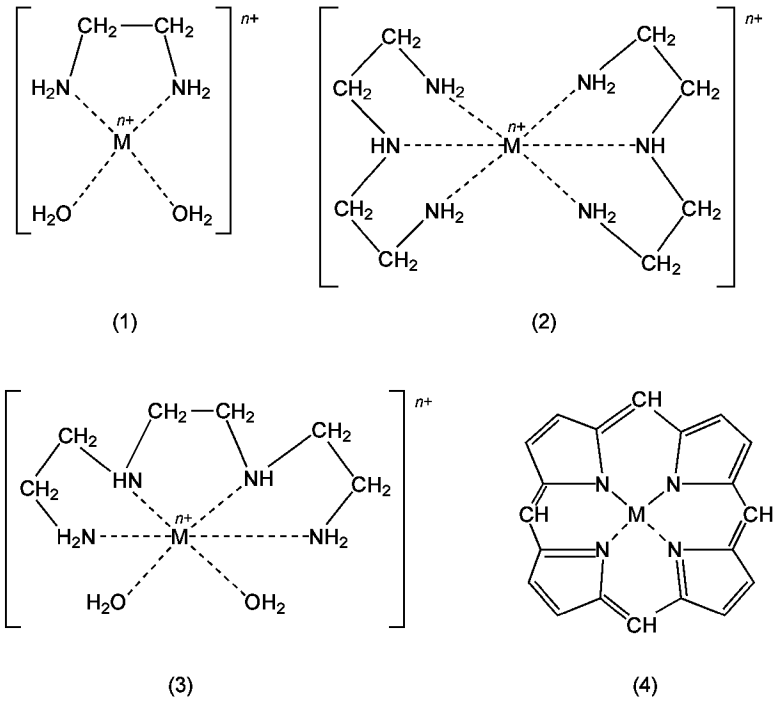


Fig. 1. Types of chelates where (1) represents a tetracoordinate metal having the bidentate chelant ethylenediamine and monodentate water; (2), a hexacoordinate metal bound to two diethylenetriamines, tridentate chelants; (3), a hexacoordinate metal having triethylenetetramine, a tetradentate chelant, and monodentate water; and (4), a porphine chelate. The dashed lines indicate coordinate bonds.

If the coordination number of M is greater than the number of donor atoms in the ligand L, more than one ligand molecule may combine with the metal to form the complex ML_n as in structure (2) where $n \geq 2$. Moreover, different chelating molecules can combine with the same metal atom to form species such as $L_mML'_n$. Remaining vacant coordination sites of the metal may also bind monodentate molecules as illustrated in (1) and (3). Solvated metal ions in water or other monodentate solvents are generally solvent coordinated and therefore, chelate formation should be regarded as a displacement of solvent molecules by the donor atoms of the chelating ligand.

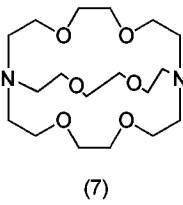
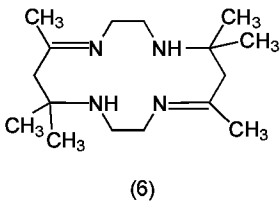
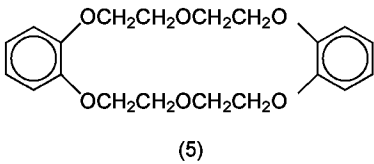
Just as a metal can coordinate with more than one chelating molecule, a ligand having enough donor atoms in the proper configuration can bind

more than one metal. These metal atoms may be the same or different.

A chelate compound may be either a neutral molecule or a complex ion associated with the appropriate counterions to produce electroneutrality. The formal charge on the complex is the algebraic sum of the charges resulting from any charge on the ligand or ligands and the charge of the metal. The ligand may be neutral or completely or partially ionized before chelation occurs. Changes in the charge of either or both metal atom and chelating agent may occur during the chelating reaction as, for example, by the displacement of hydrogen atoms or ions from the ligand donor atoms, or by an oxidation–reduction reaction between the metal and the chelant. After the chelate is formed, the charge of the complex can also change. Charge change often involves ionization of groups on the ligand that are not involved in the chelate structure, usually as a result of changes in the pH, or by oxidation or reduction of the chelated metal atom.

Most chelating agents are linear or branched chains where the donor atoms are separated by suitable numbers of other atoms to allow the formation of the chelate rings. However, there are also classes of chelating agents where the donor atoms are contained within macrocyclic structures. The spacer atoms complete the chelate rings between pairs of coordinated donor atoms, forming a pattern of fused rings centered about the metal. The porphyrins are examples of this type of chelate, and structure (4) represents chelates of porphine [101-60-0], the parent compound of the porphyrins.

Another group of macrocyclic ligands that have been extensively studied are the cyclic polyethers, such as dibenzo-[18]-crown-6 (5), in which the donor atoms are ether oxygen functions separated by two or three carbon atoms. The name crown ethers has been proposed (2) for this class of compounds because of the resemblance of their molecular models to a crown. Sandwich structures are also known in which the metal atom is coordinated with the oxygen atoms of two crown molecules.



Related to the crown ethers are compounds, such as hexamethyl-[14]-4,11-diene N₄ (6), which differ by the replacement of one or more of the oxygen atoms by other kinds of donor atoms, particularly N or S. Macrocyclic amine and thioether compounds have been synthesized. Compounds having more than one kind of heteroatom in the ring are called mixed-donor macrocycles. The naturally occurring metabolites nonactin [6833-84-7] and monactin [7182-54-9] have both ether and ester groups incorporated in the macrocyclic structure.

Three-dimensional polymacrocyclic chelating agents are formed by joining bridgehead structures with chains that contain properly spaced donor atoms. For example, bicyclic molecules result from joining nitrogen bridgeheads with chains of (–OCH₂CH₂–) groups as in 2.2.2-cryptate (7) (3). Such bicyclic structures form a cavity that holds a metal coordinated to the donor atoms in the surrounding chains. Other groups that are at least trifunctional can serve as bridgeheads, eg, pentaerythritol [115-77-5] (see ALCOHOLS, POLYHYDRIC). The donor atoms of the bridges may all be O, N, or S, or the compounds may be mixed donor macrocycles in which the bridge strands contain combinations of these donor atoms. Synthesis, metal binding, and thermodynamic properties of synthetic multidentate macrocyclic complexing agents have been reviewed (4).

Incorporating ligand groups into a cross-linked polymer structure gives the chelate-forming resins that perform ion-exchange functions by chelation. The ligand groups may either be present in the monomer before polymerization, or they may be attached to a preformed polymer by appropriate reactions. Several types are commercially available. Cross-linked styrenedivinylbenzene bonded at the nitrogen atoms to iminodiacetic acid groups is such a polymer.

Compounds Having Chelating Properties

Compounds with chelating properties can be found in almost any class of structures containing two or more donor atoms spatially situated so that they can coordinate with the same metal atom. The chelate rings formed contain four or more members, but for the same donor atoms, the five- or six-membered chelate rings are usually the most stable and most useful. Complexes having chelate rings of more than six members are rare. In the macrocyclic molecules, the stability of the metal complex depends strongly on the relationship between the size of the metal ion and the size of the opening within the crown or the crypt.

Chelating agents may be either organic or inorganic compounds, but the number of inorganic agents is very small. The best known inorganic chelants are polyphosphates. The annual consumption of these compounds exceeds that of all the organic chelating agents combined. Polyphosphates are less expensive than the organics but are hydrolytically unstable at high temperature and pH. Although many hundreds of organic chelating agents are known, only a few members of a few classes of compounds find extensive industrial use. One important class of organic chelating agents is the group of phosphonic acids analogous to the amino- and hydroxycarboxylic acids. These phosphonate chelants possess many of the complexing properties of the inorganic polyphosphates, particularly threshold-scale inhibition, effective at much less than stoichiometric ratios of chelant to metal ion, but unlike the polyphosphates, the phosphonates are stable in water at high temperature and pH.

Table 1 lists a number of chelating agents, grouped according to recognized structural classes. Because systematic nomenclature of chelating agents is frequently cumbersome, chelants are commonly referred to by common names and abbreviations. For the macrocyclic complexing agents, special systems of abbreviated nomenclature have been devised and are widely used. Some of the donor atoms involved in chelation and the many forms in which they can occur have been reviewed (5).

Table 1. Classes of Chelating Agents

Chelating agent	CAS Registry	Molecular formula	Abbreviation
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Number			
<i>Polyphosphates</i>			
sodium tripolyphosphate	[7758-29-4]	Na ₅ P ₃ O ₁₀	STPP
hexametaphosphoric acid	[18694-07-0]	H O ₁₈ P	
<i>Aminocarboxylic acids</i>			
ethylenediaminetetraacetic acid	[60-00-4]	C ₁₀ H ₁₄ N ₂ O ₈	EDTA
hydroxyethylethylenediamine-triacetic acid	[150-39-0]	C ₁₀ H ₁₈ N ₂ O ₇	HEDTA
nitrilotriacetic acid	[139-13-9]	C H ₉ NO	NTA
N-dihydroxyethylglycine	[150-25-4]	C H ₁₃ NO ₄	2-HxG
ethylenebis(hydroxyphenyl-glycine)	[1170-02-1]	C ₁₈ H ₂₀ N ₂ O	EHPG
<i>1,3-Diketones</i>			
acetylacetone	[123-54-6]	C ₅ H ₈ O ₂	acac
trifluoroacetylacetone	[367-57-7]	C ₅ H ₅ F ₃ O ₂	tfa
thenoyltrifluoroacetone	[326-91-0]	C ₈ H ₅ F ₃ O ₂ S	TTA
<i>Hydroxycarboxylic acids</i>			
tartaric acid	[526-83-0]	C ₄ H O	
citric acid	[77-92-9]	C H ₈ O ₇	cit
gluconic acid	[133-42-6]	C H ₁₂ O ₇	
5-sulfosalicylic acid	[97-05-2]	C ₇ H O S	5-SSA
<i>Polyamines</i>			
ethylenediamine	[107-15-3]	C ₂ H ₈ N ₂	en
diethylenetriamine	[111-40-0]	C ₄ H ₁₃ N ₃	dien
triethylenetetramine	[112-24-3]	C H ₁₈ N ₄	trien
triaminotriethylamine	[4097-89-6]	C H ₁₈ N ₄	tren
<i>Aminoalcohols</i>			
triethanolamine	[102-71-6]	C H ₁₅ NO ₃	TEA
N-hydroxyethylethylene-diamine	[111-41-1]	C ₄ H ₁₂ N ₂ O	hen
<i>Aromatic heterocyclic bases</i>			
dipyridyl	[366-18-7]	C ₁₀ H ₈ N ₂	dipy, bipy
o-phenanthroline	[66-71-7]	C ₁₂ H ₈ N ₂	phen
<i>Phenols</i>			
salicylaldehyde	[90-02-8]	C ₇ H O ₂	
disulfoxyrocatechol	[149-46-2]	C H O ₈ S ₂	Tiron, PDS
chromotropic acid	[148-25-4]	C ₁₀ H ₈ O ₈ S ₂	DNS
<i>Aminophenols</i>			
oxine, 8-hydroxyquinoline	[148-24-3]	C ₉ H ₇ NO	Q, ox
oxinesulfonic acid	[84-88-8]	C ₉ H ₇ NO ₄ S	
<i>Oximes</i>			
dimethylglyoxime	[95-45-4]	C ₄ H ₈ N ₂ O ₂	
salicylaldoxime	[94-67-7]	C ₇ H ₇ NO ₂	
<i>Schiff bases</i>			
disalicylaldehyde 1,2-propylenediimine	[94-91-7]	C ₁₇ H ₁₈ N ₂ O ₂	
<i>Tetrapyrroles</i>			
tetraphenylporphin	[917-23-7]	C ₄₄ H ₃₀ N ₄	
phthalocyanine	[574-93-6]	C ₃₂ H ₁₈ N ₈	
<i>Sulfur compounds</i>			
toluenedithiol (Dithiol)	[496-74-2]	C ₇ H ₈ S ₂	tdth
dimercaptopropanol	[59-52-9]	C ₃ H ₈ OS ₂	BAL
thioglycolic acid	[68-11-1]	C ₂ H ₄ O ₂ S	
potassium ethyl xanthate	[140-89-6]	C ₃ H OS ₂ ·K	
sodium diethyldithiocarbamate	[148-18-5]	C ₅ H ₁₁ NS ₂ ·NA	
dithizone	[60-10-6]	C ₁₃ H ₁₂ N ₂ S	dz
diethyl dithiophosphoric acid	[298-06-6]	C ₄ H ₁₁ O ₂ PS ₂	
thiourea	[62-56-6]	CH ₄ N ₂ S	
<i>Synthetic macrocyclic compounds</i>			
dibenzo-[18]-crown-6	[14187-32-7]	C ₂₀ H ₂₄ O	
hexamethyl-[14]-4,11-dieneN ₄	[29419-92-9]	C ₁₄ H ₃₂ N ₄	
(2.2.2-cryptate)	[23978-09-8]	C ₁₈ H ₃₄ N ₂ O	
<i>Polymers</i>			
polyethyleneimines	[9002-98-6]	(C ₂ H ₅ N) _x	PEI
	[25988-99-2]	(C ₂ H ₅ N) _x	
	[32167-41-2]	(C ₂ H ₅ N) _n C ₈ HF ₁₇ O ₂ S	
	[25120-51-8]	(C ₇ H ₁₀ O ₂) _x	
polymethacryloylacetone	[25120-51-8]	(C ₇ H ₁₀ O ₂) _x	
poly(<i>p</i> -vinylbenzyliminodiacetic acid)	[30395-28-9]	(C ₁₃ H ₁₅ NO ₄) _x	
<i>Phosphonic acids</i>			
nitrilotrimethylenephosphonic acid	[6419-19-8]	C ₃ H ₁₂ NO ₉ P ₃	NTPO, ATMP
ethylenediaminetetra-(methylenephosphonic acid)	[1429-50-1]	C H ₂₀ N ₂ O ₁₂ P ₄	EDTPO
hydroxyethylidenediphosphonic acid	[2809-21-4]	C ₂ H ₈ O ₇ P ₂	HEDP

Nomenclature and Structural Representation

Chelating Agents. Besides the conventional empirical and structural formulas, chelating compounds and chelates are often represented by type formulas, ie, formulas that show only generalized types of structural features. Chelants having proton acid groups may be shown as $H_m A^n^-$. Alcohol or phenol groups that lose protons on chelation are shown as $A(OH)_n^-$. The letter A may be used to represent an entire multidentate ligand molecule or to show only a donor atom as in $A-A-A-A$ for a tetradentate ligand.

For many macrocyclic ligands, simplified names are in common use. For example, crown ether nomenclature consists of four parts: (1) the number and type of fused rings on the polyether ring; (2) in square brackets the number of atoms in the polyether ring; (3) the word crown; and (4) the number of oxygen atoms in the macro ring (2). Ligand structures may be represented by any of the conventional means for depicting structure, eg, see structures (5–7).

Chelates. Because of length and complexity, systematic names of chelates are little used except for special purposes, such as where unequivocal referencing is essential. Chelates are named in the literature in a variety of ways. The name of the ligand in a chelate is usually given a suffix -o or -ato if it is a negative group but remains unchanged if the ligand is electrically neutral. Prefixes indicate the number of bound ligand molecules. The central atom is given the name of the metal, or a derivative name having the suffix -ate, eg, cuprate and ferrate, if the complex is negatively charged. Oxidation states of the metals are indicated by Roman numerals, eg, iron(III), and ionic charges are shown as part of the name by Ewens-Bassett numbers, eg, (2+) or (1-).

Chelates are often named merely as a complex, eg, cadmium complex with acetylacetone. A common practice in the literature is to give the symbol of the central atom and an abbreviation for the ligand with or without an indication of ionic charges, oxidation states, structure, or counterions, as in the following: Pb-EDTA, Ca-cit⁻, Cu(en)₂, Co(II)-(phen), [Cu(dipy)₃][SO₄], [Ru(dipy)₂(en)]²⁺, and Na[Co(acac)₃]. Ligand abbreviations are given in Table 1.

Several ways of representing chelates are shown in Figure 2. Structures (8) and (9) represent bidentates; structures (10) and (11), tetradentates; and structures (12) and (13) the same hexadentate. Square brackets, evident in structures (9)–(11), may be used to emphasize that the structure is a complex ion, but brackets are not a requirement. The sum of charges shows that structure (12) is also a charged (1-) complex; structure (8) is neutral. In structure (13), which is used to show spatial arrangements, the curved lines represent chains of unspecified length connecting the donor atoms. Note that the aromatic rings in (9) sterically prevent the sulfo groups from chelating with the central metal.

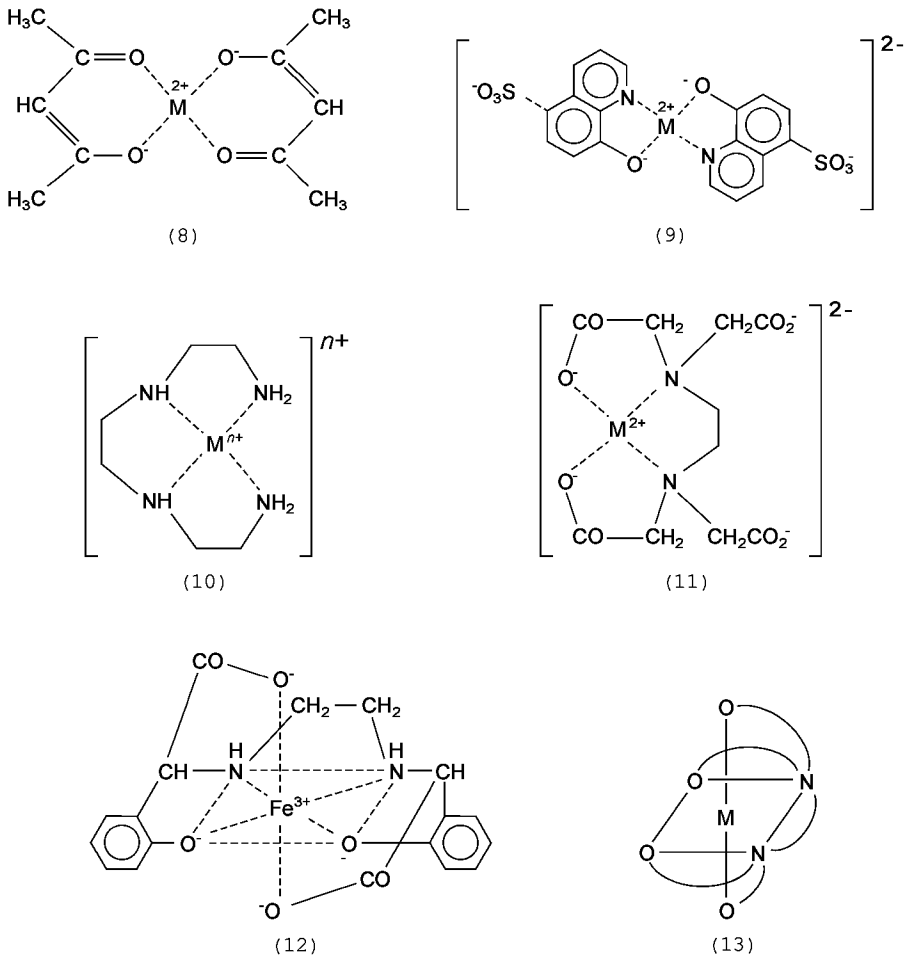


Fig. 2. Structural representations of chelates where (8) corresponds to $M(acac)_2$; (9) to ML_2^{2-} , $L = 5$ -sulfo-8-hydroxyquinoline; (10) to M -Trien; (11) to a tetracoordinate metal bound to the hexadentate ligand EDTA; and (12) to the Fe(III) chelate of EHPG. Structure (13), which emphasizes the spatial arrangement of the donor atoms, also represents the chelate in (12).

For the many details of constructing or interpreting structures and systematic names, the literature on nomenclature and indexing (6) can be consulted. Systematic nomenclature is illustrated by the *Chemical Abstracts* name of the sodium iron(III) EHPG chelate: sodium [[N,N'-1,2-ethanediylbis[2-(2-hydroxyphenyl)glycinato]](4-)-N,N',O,O',O²][ferrate(1-)] [16455-61-1]. The ferrate anion (12) [20250-28-6] and the potassium salt [22569-56-8] are also listed in *Chemical Abstracts* (7).

The Chelation Reaction

Chelate Formation Equilibria. In homogeneous solution the equilibrium constant for the formation of the chelate complex from the solvated metal ion and the ligand in its fully dissociated form is called the formation or stability constant. Whereas the ligand displaces solvent molecules coordinated to the metal, these solvent molecules do not generally enter into the equations. When more than one ligand molecule complexes with a metal atom, the reaction usually proceeds stepwise. For a metal having a coordination number of six and a bidentate chelating agent, the equations representing the equilibria are

$$M + L \rightleftharpoons ML \qquad K_1 = \frac{[ML]}{[M][L]}$$
(1)

$$ML + L \rightleftharpoons ML_2 \qquad K_2 = \frac{[ML_2]}{[ML][L]}$$

$$ML_2 + L \rightleftharpoons ML_3 \qquad K_3 = \frac{[ML_3]}{[ML_2][L]}$$

$$overall : M + 3 L \rightleftharpoons ML_3 \qquad K = \frac{[ML_3]}{[M][L]^3}$$

where the square brackets represent concentrations in units of molarity. The overall stability constant is the product of the step stability constants, ie, $K = K_1 K_2 K_3$, and is often designated by β . Protons displaced from a ligand in the chelation reaction may be shown, as in equation 5, where H_2A^{2-} represents the divalent anion of a multidentate ligand such as EDTA.

$$M^{2+} + H_2A^{2-} \rightleftharpoons MA^{2-} + 2 H^{+} \qquad k = \frac{[MA^{2-}][H^{+}]^2}{[M^{2+}][H_2A^{2-}]}$$

Such a reaction is the sum of an acid dissociation reaction

$$H_2A^{2-} \rightleftharpoons A^{4-} + 2 H^{+} \qquad K_a = \frac{[A^{4-}][H^{+}]^2}{[H_2A^{2-}]}$$

and the reaction of chelate formation from the fully dissociated form of the ligand

$$M^{2+} + A^{4-} \rightleftharpoons MA^{2-} \qquad K = \frac{[Ma^{2-}]}{[M^{2+}][A^{4-}]}$$

where K is the chelate formation constant, K_a is the overall acid dissociation constant for the two stages, and $k = K K_a$.

Experimentally determined equilibrium constants are usually calculated from concentrations rather than from the activities of the species involved. Thermodynamic constants, based on ion activities, require activity coefficients. Because of the inadequacy of present theory for either calculating or determining activity coefficients for the complicated ionic structures involved, the relatively few known thermodynamic constants have usually been obtained by extrapolation of results to infinite dilution. The constants based on concentration have usually been determined in dilute solution in the presence of excess inert ions to maintain constant ionic strength. Thus concentration constants are accurate only under conditions reasonably close to those used for their determination. Beyond these conditions, concentration constants may be useful in estimating probable effects and relative behaviors, and chelation process designers need to make allowances for these differences in conditions.

Stability constants for a number of industrially important metals and some widely used chelating agents are given in Table 2. Extensive listings of stability constants are available (8). The practical significance of formation constants is that a high log K value means a large ratio of chelated to unchelated or free metal when equivalent amounts of metal and ligand are present. From the values shown in Table 2, it is apparent that the concentration of free metal ion can range from relatively large to very low depending on the chelant.

Table 2. Concentration Formation Constants of Metal Chelates^a

Metal ion	Log K						
	STPP	Citric acid	EDTA	EDTPO	NTA		
					Log K_1	Log K_2	Log K_1K_2
V(III) ^b			25.9				
Fe(III)		10.9	25.1		15.9	9.9	25.8
In(III)			25.0		15.0	9.6	24.6
Th(IV)			23.2		12.4		
Hg(II)			21.8		12.7		
Cu(II)	8.7	6.1	18.8	23.21	12.7	3.6	16.3
Ni(II)	6.7	4.8	18.6	16.38	11.3	4.5	15.8
Y(III)			18.1		11.4	9.1	20.5
Pb(II)		5.7	18.0		11.8		
Zn(II)	7.6	4.5	16.5	18.76	10.5		
Cd(II)		4.2	16.5		10.1	4.4	14.5
Co(II)	6.9	4.4	16.3	17.11	10.6		
Fe(II)	2.5	3.2	14.3		8.8		
Mn(II)	7.2	3.4	14.0		7.4		
V(II)			12.7				
Ca(II)	5.2	3.5	10.7	9.36	6.4		
Mg(II)	5.7	2.8	8.7	8.43	5.4		
Sr(II)	4.4		8.6		5.0		
Ba(II)	3.0		7.8		4.8		
rare earths			15.1–20.0		10.4–12.5		

^a STPP = sodium tripolyphosphate; NTA = nitrilotriacetic acid; EDTA = ethylenediaminetetraacetic acid; EDTPO ethylenediaminetetra(methylenephosphonic acid) (see Table 1).

^b The oxovanadium(IV) ion, VO²⁺, forms a complex with EDTA having log $K = 18.8$.

Many experimental approaches have been applied to the determination of stability constants. Techniques include pH titrations, ion exchange, spectrophotometry, measurement of redox potentials, polarimetry, conductometric titrations, solubility determinations, and biological assay. Details of these methods can be found in the literature (9,10).

Displacement Equilibria. Species in solution are generally in formation—dissociation equilibrium, and displacement reactions of any given metal or ligand by another are possible. Thus,



or



If the stability constants for ML and M'L are K and K' , respectively, then for the exchange shown in equation 8, the equilibrium constant is K_x .

$$K_x = \frac{[M][M'L]}{[ML][M']} = \frac{K'}{K} \tag{10}$$

The extent of displacement depends on the relative stabilities of the complexes and the mass action effect of an excess of M'. For equivalent total amounts of M and M', K_x must be on the order of 10^4 for 99% complete displacement to occur. Similar considerations apply for the displacement of L from ML by L'. The situation is quite analogous to the familiar competition of two bases for the hydrogen ion.

If the metals or ligands involved in a displacement reaction form chelates where type formulas are different, the exchange equilibrium constant is the simple ratio of the formation constants of the chelates. Rather, for the reaction



the equilibrium constant $K_x = K'/K^2$ assuming K and K' are the respective formation constants of ML and M'L₂. The proper evaluation of K_x can be derived for each particular case.

Metal exchange is the mechanism by which many foods, such as shortenings, shellfish, and dairy products, are stabilized against deleterious effects of trace metals by the addition of Na₂CaEDTA (log $K = 10.7$). Copper (log $K = 18.8$) and iron (log $K = 25.1$) displace calcium and become sequestered so that the remaining concentration of free iron or copper ions is too low for catalytic effects to occur at significant rates (11). Ligand exchange occurs when ascorbic acid [50-81-7] bound to copper (log $K = 1.57$) is displaced by EDTA, stabilizing this vitamin by disrupting an oxidation mechanism (12). Dyes and bleaches are similarly protected in the textile industry (13) (see FOOD ADDITIVES; DYES AND DYE INTERMEDIATES; BLEACHING AGENTS).

The addition of a chelating agent to a solution of two or more metal ions leads to an order of metal ion complexation that is regulated by the displacement equilibrium constants. If the objective is to bind only a particular ion, then enough chelant to combine with the target ion and all the other ions that are capable of displacing the target ion should be added. For any particular chelating agent under similar solution conditions, a displacement series of metal ions can be assembled by calculating the K_x values from series of stability constants such as those in Table 2. For selective complexation of one metal in the presence of another, a chelating agent with sufficiently different stability constants for the two metals is necessary so that K_x becomes large. For example, beryllium occurs at the bottom of a displacement series with NTA allowing this metal to be recovered as the hydroxide by pH adjustment of an ore processing solution; all of the interfering metals remain sequestered by chelation (14). Additionally, because other metals present cannot displace iron in an iron-EHPG chelate, the chelate can be used in highly calcareous soils to supply iron as a trace nutrient in agriculture (15).

Selectivity for a single metal of a group is the basis of a solvent extraction process for the recovery of copper (qv) from low concentration ore leach solutions containing high levels of iron (qv) and other interfering metals (16).

Rates of Reaction. The rates of formation and dissociation of displacement reactions are important in the practical applications of chelation. Complexation of many metal ions, particularly the divalent ones, is almost instantaneous, but reaction rates of many higher valence ions are slow enough to measure by ordinary kinetic techniques. Rates with some ions, notably Cr(III) and Co(III), may be very slow. Systems that equilibrate rapidly are termed kinetically labile, and those that are slow are called kinetically inert. Inertness may give the appearance of stability, but a complex that is apparently stable because of kinetic inertness may be unstable in the thermodynamic equilibrium sense.

Factors Affecting Stability. A characteristic of chelation distinguishing it from monodentate metal coordination is the increased stability from ring formation of the resultant chelate complex. For equal numbers of similar coordinated donor atoms, as in amine complexes compared to chelates of ethylenediamine, eg, M(RNH₂)₂ vs M(en) or M(RNH₂)₄ vs M(en)₂, the stability constants of the chelates are from one to several orders of magnitude greater than those of the monodentate complexes. The greater stability of the chelates is largely the result of an increase in entropy resulting from an increase in the number of free molecules, usually solvent or other monodentate ligand, liberated as the chelate is formed. This extra stabilization produced by the ring formation is called the chelate effect.

Many parameters influence the stability of chelates. Several of the stability factors common to all chelate systems are the size and number of rings, substituents on the rings, and the nature of the metal and donor atoms. In the macrocyclic complexes, the degree to which the size of the metal ion fits the space enclosed by the macro rings is a significant factor. In chelation, five- and six-membered rings are most stable: coordination angles on the metal atoms prohibit the formation of three-membered rings, and ring closure is improbable for rings having more than seven members. In these latter systems, coordination in linear chains is a competing reaction. Formation of each additional ring by the same ligand contributes extra stability from the entropy effect of displacing coordinated solvent molecules. Substituents on a ring may also produce steric hindrance, or otherwise alter the availability of the donor atom electrons for coordination.

The alkaline and rare-earth metals, and positive actinide ions, generally have greater affinity for –O– groups as electron donors. Many transition metals complex preferentially with enolic –O– and some nitrogen functions. Polarizability of the donor atoms correlates with stability of complexes of the heavier transition metals and the more noble metal ions.

In any series of chelates, the stability constants are usually influenced by more than one of the parameters that are known to affect chelate stability. The data in Table 3 illustrate some of these relationships: the calcium complexes containing EDTA and homologues decrease in stability as the size of the chelate ring formed by the metal and the two coordinating nitrogen atoms increases. The aminoacetic acid series shows the stability gained from the formation of additional rings on a single-ligand molecule. And the copper–polyamine series shows the combined effects of ring size, number of rings for similar donor atoms, and whether the rings are formed by one or more ligand molecules.

Table 3. Ring Effects on Complex Stability

Ligand, L	Complex formula	Ring size	Number of rings	Number of coordinated donor atoms	Log K^a		
EDTA, $n = 2^b$	CaL	5			10.5		
homologue, $n = 3^{b,c}$	CaL	6			7.1		
homologue, $n = 4^{b,d}$	CaL	7			5.2		
homologue, $n = 5^{b,e}$	CaL	8			4.6		
					Cu(II)	Ni(II)	Co(II)
H ₂ NCH ₂ COOH ^f	ML	5	1	2	8.6	6.2	5.2
HN(CH ₂ COOH) ₂ ^g	ML	5	2	3	10.6	8.2	7.0

N(CH ₂ COOH) ₃	ML	5	3	4	12.7	11.3	10.6
					Log <i>K</i> ₁	Log <i>K</i> ₂	Log <i>K</i> ^h
H ₂ NC ₂ H ₄ NH ₂	CuL	5	1	2	10.72		
	CuL ₂	5	2	4		9.31	20.0
H ₂ N(CH ₂) ₃ NH ₂ ⁱ	CuL	6	1	2	9.77 ⁱ		
	CuL ₂	6	2	4		7.1	16.9 ^j
HN(C ₂ H ₄ NH ₂) ₂ ^k	CuL	5	2	3	15.9		
	CuL ₂	5	2	4		5.4	21.3
(H ₂ NC ₂ H ₄ NHCH ₂) ₂	CuL	5	3	4	20.5		

^a Ref. 9.

^b Formula is (HOOCCH₂)₂ N(CH₂)_{*n*} N(CH₂COOH)₂.

^c Propylenedinitrilotetraacetic acid [1939-36-2], C₁₁H₁₈N₂O₈.

^d Tetramethylenedinitrilotetraacetic acid [1798-13-6], C₁₂H₂₀N₂O₈.

^e Pentamethylenedinitrilotetraacetic acid [1798-14-7], C₁₃H₂₂N₂O₈.

^f Glycine [56-40-6], C₂H₅NO₂.

^g Iminodiacetic acid [142-73-4], C₄H₇NO₄.

^h Log *K* = Log *K*₁ + *K*₂.

ⁱ 1,3-Propanediamine [109-76-2], C₃H₁₀N₂.

^j Ref. 10.

^k N-2-Aminoethyl-1,2-ethanediamine [111-40-0], C₄H₁₃N₃.

pH Effects. Being Lewis bases, the donor atoms of chelating agents react with Lewis acids such as metal and hydrogen ions. In the pH range of aqueous solutions, most of the well-known chelating agents exist as an equilibrium mixture of both protonated and unprotonated forms. Metal ions compete with hydrogen ions for the available donor atoms, and therefore, simultaneous equilibria exist that are treated mathematically by the simultaneous equations for the formation constants of the chelates and the acid dissociation constants of the chelating agents.

In aqueous systems, water is a competing ligand, and its dissociation into hydrogen and hydroxyl ions must often be considered in the system of simultaneous equilibria (see HYDROGEN ION ACTIVITY). In nonaqueous solvents, similar treatment is possible with appropriate modifications for the acidity in those systems. The pH leveling effect of water affects and limits the acid dissociation behavior of chelating agents in aqueous systems. However, coordination with certain metals in aqueous solution can result in loss of a proton from aliphatic -OH and -NH₂ groups.

Consider the equilibria in an aqueous system composed of a bidentate ligand HA, eg, the enol form of acetylacetone, and a tetracoordinate metal M²⁺, structure (8). The equations are

$$HA \rightleftharpoons A^- + H^+ \qquad K_a = \frac{[H^+][A^-]}{[HA]}$$

$$M^{2+} + 2 A^- \rightleftharpoons MA_2 \qquad K = \frac{[MA_2]}{[M^{2+}][A^-]^2}$$

giving the relation

$$[M^{2+}] = \frac{[H^+]^2}{[HA]^2} \times \frac{[MA_2]}{K K_a^2}$$

Equation 14 shows that an increase in acidity of the solution increases the concentration of uncomplexed metal, which must result from the displacement of M²⁺ from MA₂, causing a simultaneous decrease in the ratio of complexed to free ligand [MA₂]/[HA]. The opposite effects result upon decreasing the acidity. This behavior occurs in the pH range where appreciable amounts of both HA and A⁻ coexist. Outside this range the ligand is present almost entirely as either HA or MA₂ and A⁻, and the system is essentially independent of pH.

Chelating agents that are polybasic acids give two or more hydrogen ions per molecule. The four stages of dissociation of EDTA, eg, are represented by the equations

$$H_4A \rightleftharpoons H^+ + H_3A^- \rightleftharpoons H^+ + H_2A^{2-} \rightleftharpoons H^+ + HA^{3-} \rightleftharpoons H^+ + A^{4-}$$

These equilibrium constants *K*₁, *K*₂, *K*₃, and *K*₄ are known (10). The p*K* values for the four dissociation steps as well as the proportions of the species present in aqueous solution as a function of pH are shown in Figure 3. The reaction of Na₂EDTA and M²⁺, represented by equation 5 and noting that *K*₁ *K*₃ *K*₄ = *k*, give

$$[M^{2+}] = \frac{[H^+]^2}{[H_2A^{2-}]} \times \frac{1}{K K_3 K_4}$$

which is of the same form as equation 14. In general, for the reaction

$$[M^{x+}] + H_n A^{y-n} \rightleftharpoons [MA^{x-y-n}] + n H^+$$

the equation for the concentration of free metal is

$$[M^{x+}] = \frac{[H^+]^n}{[H_n A^{y-n}]} \times \frac{1}{KC}$$

where *K* is the formation constant (eq. 7) of MA^{*x-y-n*} and *C* is the product of the *n* stepwise acid dissociation constants involved. Taking the negative logarithm of both sides of the equation and letting -log [M^{*x+*}] = p*M*, the equation becomes

$$pM = n \text{ pH} + \log \frac{[H_n A^y]}{[MA^{x-y-n}]} + \log KC \tag{19}$$

The corresponding generalized form for equation 14 is

$$pM = n \text{ pH} + \log \frac{[HA]^n}{[MA_n^{x-n}]} + \log K K_{a^n} \tag{20}$$

In both cases n is the number of hydrogen ions displaced in the formation of the complex. In solutions where the ratio of free chelating agent to complex, $[H_n A^y] / [MA^{x-y-n}]$, is held constant, the slopes of the curves pM vs pH are equal to n in the region where $H_n A^y$ is the principal form of the chelating agent.

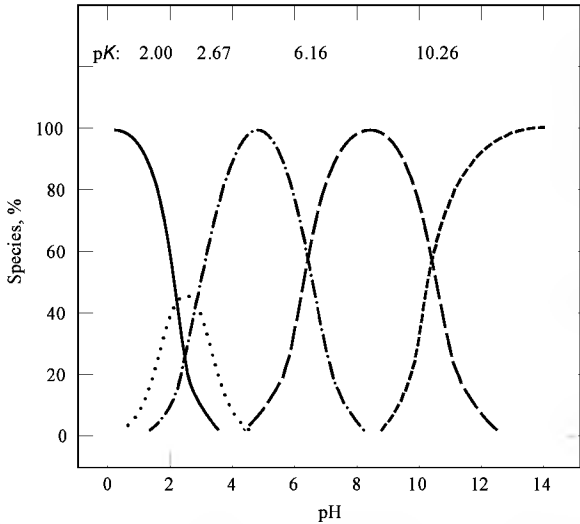
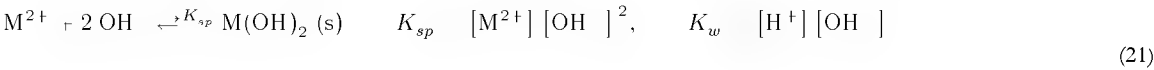


Fig. 3. Distribution of ionic species of EDTA as a function of pH where (—) represents H_4A , ($\cdots$) H_3A^- , ($-\cdots-$) H_2A^{2-} , ($----$) HA^{3-} , and ($-----$) A^{4-} .

The displacement of hydrogen ions by a metal ion from a protonated form of the chelating agent (eq. 17) generates an autogenous pH that depends on the base strength of the counterions of the metal salt. The pH of the solution can become quite low if these counterions are those of a strong acid, eg, Cl^- or SO_4^{2-} . However the pH of chelate solutions can be controlled by the use of compatible buffers, and the chelating agent itself can sometimes serve as the pH buffer if one of its acid dissociation stages occurs in the desired pH range.

The variation of pM with pH according to equation 17 is shown in Figure 4 for EDTA and Cu(II) and EDTA and Mn(II) at three different ratios of free chelant to metal chelate, $[H_n A^y] / [MA^{x-y-n}]$. The pM value at any pH indicates the concentration of the free aquo metal ion in equilibrium with the chelate. From pH 2 to 6, the free form of the EDTA is H_2A^{2-} , and because two protons are displaced by the metal on chelation, the slope of the curves is two. The slope changes to one from pH 6 to 10 where the EDTA is present as HA^{3-} and only one proton is displaced. Above pH 10, the chelates are formed from the fully dissociated chelant, A^{4-} , no hydrogen ions are displaced, the slope of the curves is zero, and pM is independent of pH up to the pH of the intersection of the solid lines with the dashed lines for the same metal. Up to pH 10, the rise of pM with pH shows the increasing degree of metal binding as competition by hydrogen ions for the chelant is decreased. Cu(II) and Mn(II) form insoluble metal hydroxides to which the following applies at equilibrium in aqueous solution:



and from these

$$pM = 2 \text{ pH} + \log (K_w^2 / K_{sp}) \tag{22}$$

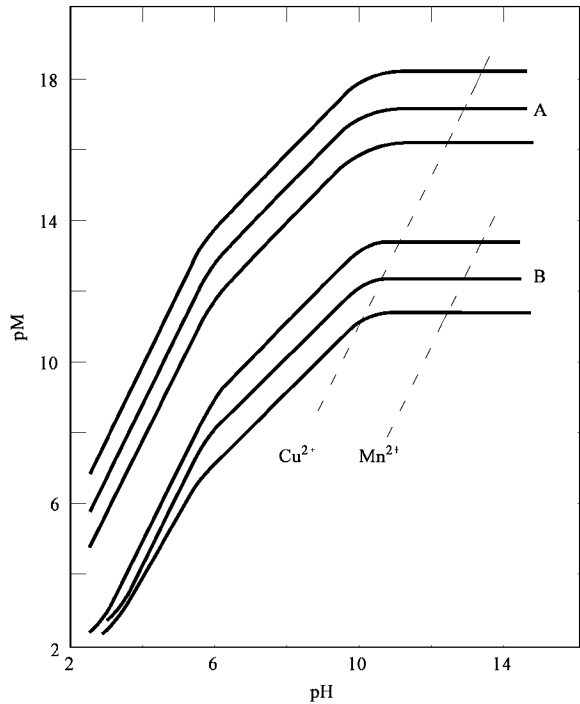


Fig. 4. pM vs pH for A: Cu(II), and B: Mn(II) EDTA chelates. For each family of curves, the lowest curve represents 1% ; the second, 10% ; and the top curve, 100% of free ligand species in excess of the amount needed to form the metal chelate. Broken lines represent solid–solution equilibria for corresponding metal hydroxides. See equation 22.

The dashed lines in Figure 4 are plots of equation 22 for Cu^{2+} and Mn^{2+} and indicate the concentration of the aquo metal ions in equilibrium with the solid hydroxides as function of pH. At any pH where the solid curve is above the dashed line for the same metal, the EDTA is holding the unchelated metal ion concentration at a value too low for the precipitation of the solid hydroxide. Relatively large quantities of the metal can thus be maintained in solution as the chelate at pH values where otherwise all but trace quantities of the metal would be precipitated. In Figure 4, this corresponds to pH values where pM of the dashed curves is 4 or greater. At the pH of intersection of the solid and dashed lines for the same metal, the free metal ion is in equilibrium with both the solid hydroxide and the chelate. At higher pH the hydroxyl ion competes more effectively than the chelant for the metal, and only a trace of either the chelate or the aquo metal ion can exist in solution. Any excess metal is present as solid hydroxide.

The more stable the chelate, the higher the pM that it can maintain, and the higher the pH required to precipitate the metal hydroxide. From equation 22 it can be seen that the smaller the solubility product K_{sp} , ie, the more insoluble the metal hydroxide, the higher the pM that a chelant must maintain to prevent precipitation. The stability constant of the Fe(III)–EHPPG complex (12), is so large (10^{35}) that iron is not precipitated even in strongly alkaline solutions.

If instead of hydroxyl ion the precipitating agent is the anion of an acid stronger than or comparable in strength to the chelating agent, the metal salt may be insoluble at low pH where the chelant is protonated but not the precipitant anions, and soluble at higher pH where the complexing form of the ligand is relatively more available. Solutions of oxalate, EDTA, and Ca(II) show this behavior; Figure 5 shows the relationships of pM to pH. The solid lines give pM for the Ca–EDTA system, and the dashed lines represent the calcium oxalate [563-72-4] CaC_2O_4 , solubility. As in Figure 4, at pH values where the dashed lines are above the solid lines, the metal is present almost entirely as the insoluble salt. To the right of the intersections of dashed and solid lines the metal is almost entirely chelated, and the solid salt phase cannot exist.

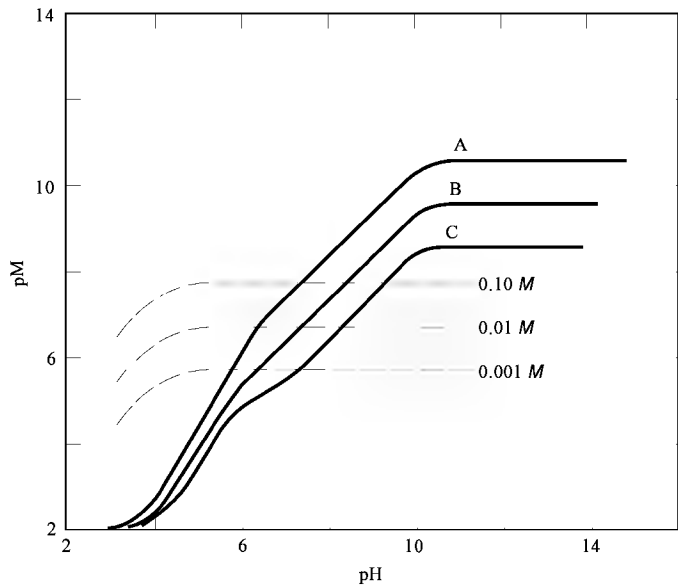
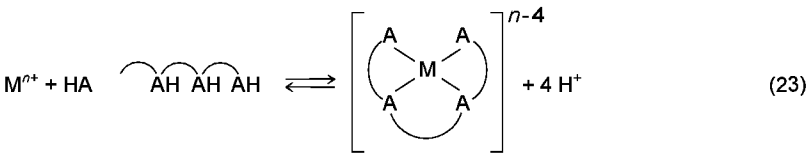


Fig. 5. pM vs pH for M = Ca(II), L = EDTA, in the presence of excess oxalate. Solid lines A, B, C represent 100%, 10%, and 1% excess EDTA, respectively. Broken lines indicate solid–solution equilibria of calcium oxalate in the presence of dissolved oxalate.

Titration Behavior. Protonated chelating agents exhibit titration behavior typical of their respective acidic groups, eg, carboxyl phenolic hydroxyl, ammonium, or sulphydryl moieties, if they are titrated with bases where the cations have a very weak or no tendency to form chelates. In the presence of a metal ion that coordinates with the donor atom of one of these acidic groups, hydrogen is displaced by the metal, and the acid strength of the group appears to be enhanced. The hydrogen ion concentration is then higher than in the absence of the metal. Strongly chelated metal ions can increase the acidity of an acidic group by several orders of magnitude. With A representing donor groups, which may be the same or different, the release of

hydrogen ions is shown schematically by



In the absence of metal coordination the compound H₄A₄ would titrate as a typical tetrabasic acid having a stepwise titration curve as shown in Figure 6. Upon strong chelation, all four protons are displaced and base titration resembles that of a typical strong acid at four times the equivalent concentration. This statement is in agreement with equation 19, which shows that pM can be large (low concentration of free metal) at low pH if K is large (strong chelation).

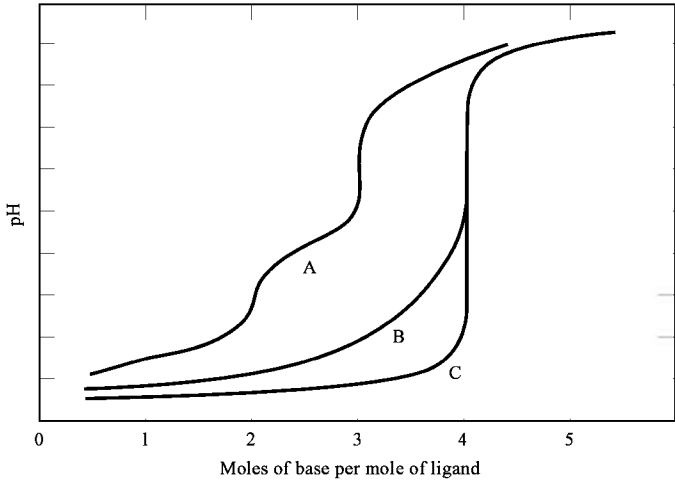


Fig. 6. Base titration of H₄A chelant: A, free acid without coordinating metal; B, in the presence of a metal of intermediate coordinate strength; and C, in the presence of a strongly chelated metal.

If metal chelation is intermediate in strength, the chelation of the groups that are last to coordinate to the metal may not do so to completion at the low pH generated by the hydrogen ions released from the first groups to coordinate. Then, in accordance with equation 19, because K is smaller, the completion of the chelation reaction, as shown by the reduction of the metal ion concentration to a low value (high pM), may not occur until a higher pH is attained where more A-groups are available to the metal. The curve of pH vs base added thus rises sooner than the curve for strong chelation, resembling the titration curve of a weak acid and reflecting the lower apparent acid strength resulting from weaker coordination. The intermediate curve of Figure 6 shows this effect of weaker chelation.

Titration of the hydrogen ion liberated from a strong chelating agent is used to determine the concentration of metal ions in solution. The strength of chelation can also be determined from these data.

Deprotonation of enols of β-diketones, not considered unusual at moderate pH because of their acidity, is facilitated at lower pH by chelate formation. Chelation can lead to the dissociation of a proton from as weak an acid as an aliphatic amino alcohol in aqueous alkali. Coordination of the O atom of triethanolamine to Fe(III) is an example of this effect and results in the sequestration of iron in 1 to 18% sodium hydroxide solution (Fig. 7). Even more striking is the loss of a proton from the amino group of a gold chelate of ethylenediamine in aqueous solution (17).

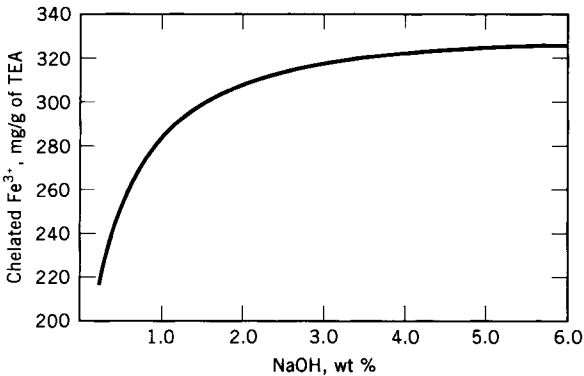


Fig. 7. Chelation of iron by triethanolamine (TEA) in aqueous sodium hydroxide.

Courtesy of The Dow Chemical Company.

Another group of chelants that form stable chelates at high pH because of metal–alkoxide coordination are the sugar acids, such as gluconic acid [526-95-4], C₆H₁₂O₇ (18). Utility for this group is found in high alkalinity bottle washes and other cleansers (19).

Metal Buffering. The equation for the formation constant of the reaction

$$M^{n+} + L^m \rightleftharpoons K ML^{n-m} \quad (24)$$

can be rearranged to give

$$\frac{1}{[M^{n+}]} = \frac{K[L^{m-}]}{[ML^{n-m}]} \quad (25)$$

from which, on taking logarithms and defining pM = -log[Mⁿ⁺],

$$pM = \log \frac{[L^m]}{[ML^{n-m}]} + \log K$$

(26)

The concentration of the metal ion can be controlled by adjusting the ratio of the concentrations of free ligand and metal chelate. If both species are present in appreciable amounts, moderate changes in either concentration have little effect on the ratio. The concentration of the metal ion can thus be buffered in a manner analogous to the buffering of pH by the presence of a weak acid and its anion

$$pH = \log \frac{[A]}{[HA]} + pK_a$$

(27)

In the equation for pM, log *K* appears instead of p*K* because *K* is a formation constant, the reciprocal of the chelate dissociation constant, which is analogous to the acid dissociation constant *K*_a.

By choice of chelating agents, and thus log *K*, pM can be regulated over a wide range. Two or more metals may be selectively buffered at different concentrations by a single chelating agent having different stability constants for the metals. Selective buffering of one metal to a low concentration in the presence of other metals is termed masking. It is the ability to maintain a nearly constant concentration of metal ions at almost any level of concentration that is the basis of many of the commercial uses of chelating agents. The buffering capacity may be used to supply metal ions at a definite concentration as in electroplating (qv) and in nutrient media (see MINERAL NUTRIENTS), or to remove or sequester metal ions in cleaning baths where the fresh stock entering the bath continually introduces additional amounts of metals.

The effect of pH on metal buffering is shown by equations 19 and 20. If a constant pH is imposed on a system by a hydrogen ion buffer, variations in pM are controlled only by variations in the ratio of the free and metal-bound forms of the ligand, and of course by the characteristics of the ligand. The free form of the ligand is the acid form its acidic dissociation stage at the imposed pH, ie, HA or H_nA^{*y*}. If the acid groups of the chelating agent are fully dissociated at the pH of the buffer, no hydrogen ions are displaced when chelation with the metal occurs, no dissociation constants of the ligand are involved, *n* in the equations is essentially zero, and pM is independent of pH. Equations 19 and 20 then reduce to the form of equation 26.

Solubilization. The solubility product of a slightly soluble salt determines the concentration of metal ion that can be present in solution with the anion of that salt. For the salt MX the solubility product is

$$K_{sp} = [M^{n+}][X^{n-}]$$

(28)

from which is obtained

$$pM = \log [X^{n-}] - \log K_{sp}$$

(29)

The presence of a sufficiently strong chelating agent, ie, one where *K* in equation 26 is large, keeps the concentration of free metal ion suppressed so that pM is larger than the saturation pM given by the solubility product relation (eq. 29) and no solid phase of MX can form even in the presence of relatively high anion concentrations. The metal is thus sequestered with respect to precipitation by the anion, such as in the prevention of the formation of insoluble soaps in hard water.

Deposits of an insoluble salt can be dissolved as a salt of the metal chelate.



In the presence of the chelating agent and the insoluble salt, MX, pM of the solution is subject to both the metal buffering and the solubility equilibria. Equating the right-hand sides of the equations 26 and 29 and rearranging gives

$$\log [X^n] = \log \frac{[L^m]}{[ML^{n-m}]} + \log K K_{sp}$$

(31)

As the dissolving of the salt progresses [Xⁿ⁻] is approximately equal to [ML^{n-m}], and both represent the amount of MX dissolved. Substituting [ML^{n-m}] for [Xⁿ⁻] in equation 31 gives

$$2 \log [ML^{n-m}] = \log [L^m] + \log K K_{sp}$$

(32)

for the equilibrium concentrations for the process. If *K K*_{*sp*} = 1, log *K K*_{*sp*} = 0, then [ML^{n-m}] = [L^m]^{1/2}, and the amount of MX solubilized is equal to the square root of the amount of excess chelating agent required, which is an amount that is in the practical range. A dilution–efficiency effect can be calculated from this relationship. If the amount of MX dissolved gives only a 0.1 *M* solution of [ML^{n-m}], the excess ligand concentration is 0.01 *M* and almost 90% of the total amount of ligand is effective in solubilizing salt deposit. However, for [ML^{n-m}] = 1.0 *M* an equal concentration of excess ligand is required and solubilization to 2.0 *M* requires 4.0 *M* excess ligand, giving efficiencies of 50 and 33%, respectively. If for economic reasons the chelating agent must be recovered, dilution is a disadvantage, and dilution and efficiency must be compromised. If the stability constant *K* is large enough, equation 32 shows that only small amounts of the chelating agent in excess of that bound to the metal are required to dissolve a given amount of the deposit.

The product *KK*_{*p*} is equal to the equilibrium constant *K*_{*f*} for the reaction shown in equation 30. It is generally considered that a salt is soluble if *K*_{*s*} > 1. Thus sequestration or solubilization of moderate amounts of metal ion usually becomes practical as *K*_{*f*} approaches or exceeds one. For smaller values of *K*_{*f*}, the cost of the required amount of chelating agent may be prohibitive. However, the dilution effect may allow economical sequestration, or solubilization of small amounts of deposits, at *K*_{*f*} values considerably less than one. In practical applications, calculations based on concentration equilibrium constants can be used as a guide for experimental studies that are usually necessary to determine the actual behavior of particular systems.

The *K*_{*f*} values for some common scale deposits and nitrilotriacetic acid (NTA), which is an effective agent for solubilizing CaSO₄ and CaSiO₃ (*K*_{*s*} > 1), are shown in Table 4. For removal of CaCO₃ deposits, a stronger Ca(II) chelating agent would be required. A large cleaning business that services industry is based on the aminocarboxylic acid chelants.

Table 4. *K*_{*s*} values for NTA and Calcium Salts^a

Salt	<i>K</i> _{<i>p</i>}	<i>K</i> _{<i>f</i>}
CaSO ₄	6.1 × 10 ⁻⁵	152
CaSiO ₃	6.6 × 10 ⁻⁷	1.65
CaCO ₃	8.7 × 10 ⁻⁹	0.022

^a Formation constant *K* = 2.5 × 10⁶.

Electrochemical Potentials. The oxidation potential of a solution containing a metal in two of its valence states, M^{x+} and M^{x+n+} , is given by

$$E = E^0 - \frac{RT}{nF} \ln \frac{[M^{x+n+}]}{[M^{x+}]}$$

(33)

In the presence of a chelating agent, the concentrations of the two forms of the metal are buffered according to the simultaneous equations

$$[M^{x+n+}] = \frac{[M_{ox}L]}{K_{ox}[L]} \quad \text{and} \quad [M^{x+}] = \frac{[M_{red}L]}{K_{red}[L]}$$

(34)

where $M_{ox}L$ and $M_{red}L$ are the chelates of the oxidized and reduced forms of the ions and K_{ox} and K_{red} are the respective formation constants. Substituting these values in the potential equation gives

$$E = E^0 + \frac{RT}{nF} \ln \frac{K_{ox}}{K_{red}} - \frac{RT}{nF} \ln \frac{[M_{ox}L]}{[M_{red}L]}$$

(35)

The first two terms of the right-hand side of the equation are sometimes combined and expressed as $E^{0'}$, which is called the standard oxidation potential for the chelate system. If the chelation is strong and the ligand is in excess, the metal would be almost entirely in the chelated forms, and $[M_{ox}L]$ and $[M_{red}L]$ would essentially be equal to the total concentrations of the oxidized and reduced forms of the metal. If, as is usual, the oxidized form is the more strongly chelated ($K_{ox} > K_{red}$), the oxidation potential of a system is increased by the addition of the chelant.

In electrodeposition, the reduced form of the metal is the elemental form M , $x = 0$, and there is no chelated M in solution. Neglecting activity coefficients, the reversible potential is

$$E = E^0 - \frac{RT}{nF} \ln [M^{x+}]$$

(36)

By buffering the metal ion concentration using a chelant, E can be adjusted to and stabilized at values that give desirable properties to the deposit. Selective buffering can sequester the properties of interfering ions or can be used to regulate the potentials of two or more ions to approximately the same value in order to effect codeposition.

Applications

Three features of chelation chemistry are fundamental to most of the applications of the chelating agents. The first and probably the most extensively used feature is the control of free metal ion concentration by means of the binding–dissociation equilibria. The second, often called the preparative feature, is that in which the special properties of the chelate itself provide the basis of the application. The third feature comprises displacement reactions: metal by other metal ions, chelant by chelant, and chelant by other ligands or ions. An application may be termed defensive if an undesirable property in a process or product is mitigated, or aggressive if a new and beneficial property is induced.

Concentration Control. Sequestration, solubilization, and buffering depend on the concentration control feature of chelation. Traces of metal ions are almost universally present in liquid systems, often arising from the materials of the handling equipment if not introduced by the process materials. Despite very low concentrations, some trace metals produce undesirable effects such as coloration or instability.

Sequestration. The suppression of certain properties of a metal without removing it from the system or phase is called sequestration. Sequestration is invaluable in controlling trace ion effects. Chelation produces sequestration mainly by reducing the concentration of free metal ion to a very low value by converting most of the metal to a soluble chelate that does not possess the properties to be suppressed. A sufficiently large stability constant in the medium of the application is required, and the sequestering agent must not cause any undesirable change that would render the system unsuitable for its intended purpose.

The largest single use for sequestration is probably the control of water (qv) hardness. Chelating agents are used to prevent the formation of precipitates in a wide variety of aqueous systems such as washing solutions of soaps (qv) and detergents, boiler feed water (20), fabric (21) and paper (qv) processing solutions (22), preparations of cosmetics (qv) and pharmaceuticals (qv), photographic developing solutions, chemical process water, beverages, and foodstuffs (18). Oil-soluble sequestrants suppress metal-catalyzed development of rancidity, gum formation in fuels, and other oxidative degradations (23). In fabric bleaching, catalytic decomposition of bleaching agents (qv) is reduced, and tenderizing of fabrics is minimized by the sequestration of metals that catalyze the reaction of the bleach with the material (24). In dyeing, metal contaminants that cause spotting, off-color shades, and decomposition of the dyes are sequestered (25). Brightness reversion in paper pulp is diminished (26), and iron is removed in the caustic washing step of the preparation of photographic and other special grades of paper. Discoloration of leather (qv) by metal-tannin complexes is prevented. Chelants are used in many metal treating operations such as phosphatizing, alkaline derusting, and etching (see METAL SURFACE TREATMENTS). Poisoning by metal ions in mammals is also treated by sequestration. Other examples can be found in the literature on sequestration and chelation.

Solubilization. Causing the constituents of a phase that is normally insoluble to dissolve in the medium is termed solubilization. Chelation solubilization depends on the formation of a chelate having groups that confer solubility in the medium and a stability sufficient to sequester the metal ion to a concentration (pM) that can exist in the presence of the associated counterions. Usually solubilization into an aqueous phase is thought of in connection with chelation. The donor atoms involved in the chelation may be sufficiently hydrophilic to produce a soluble species, as in structures (10) and (12). If the organic group is large, more hydrophilic groups may be required for water solubility. Oxine is a well-known precipitant, but its sulfonated derivative, shown in structure (9) (Fig. 1), is a solubilizer in water. A neutral chelation complex, such as structure (8), may be solubilized in organic media. The macrocyclic chelates have solubility in both aqueous and organic media as a result of their ionic nature and the largely organic character of the complex.

Dissolving hardness scale from the surfaces of boilers, heat exchangers, and piping (see PIPING SYSTEMS) is probably the largest industrial example of solubilization (27). The cleaning of films from dairy equipment and reusable beverage bottles is also a significant use (19). Deposits on processing tanks that are unique to a particular industry, such as paper, textiles (qv), metal treating, or photography (qv), are often removed by solubilization. Prevention of metal deposition by sequestration is usually preferred where possible because solubilization is sometimes slow and can lead to costly down time. Chelants are used in recovery of metals from ores (28) and in cleaning oxide films from metals in preparation for surface treatments (29). Chelation solubilization is especially useful for cleaning up radioactive contamination.

Macrotetrolides of the valinomycin group of electrically neutral antibiotics form stable 1:1 complexes with alkali metal ions that increase the cation permeability of some biological and artificial lipophilic membranes. This solubilization process appears to have implications in membrane transport research (30) (see ANTIBIOTICS, PEPTIDES).

Buffering. If addition or removal of an appreciable amount of a metal ion produces only a relatively small change in the concentration of that ion in a solution, the solution is buffered with respect to the ion. Metal ions are buffered by chelants of various strengths, ie, stability constants, in a manner exactly analogous to the buffering of hydrogen ions by bases of various strengths.

Chelation buffering is particularly useful in supplying micronutrient metal ions to biological growth systems at controlled, very low concentrations (31). At the very small subtoxic concentrations required for some metals, the amount present would ordinarily soon be depleted, but using the buffer, a reserve supply of the metal as its chelate is available over long periods with automatic control of the concentration. Examples of this kind of use are found in microorganism cultures in closed, controlled systems and in field use in agriculture in open environments (32). The metal concentration can be held at optimum values in electroplating, and chelates have supplied the metal in electroless depositions.

Control of concentrations enables simultaneous deposition of metals in alloy plating. Increasing attention is being given to the use of chelants to replace cyanide in electroplating baths. Chelants are used to control the activity of redox polymerization catalysts by buffering the metal ions participating in the mechanism. Buffering of the metal is produced by having appreciable amounts of both the chelant and the chelate present simultaneously. The pM is determined mainly by the stability constant of the chelate, and within the region of this primary regulation over a small practical range, by the ratio of chelant and chelate concentration.

Special Properties of Chelates. Some of the principal applications of the preparative feature of chelation depend on the solubility properties, color, or catalytic effects of the chelates. Selection of a chelant to form a chelate that is soluble in the medium enables the solubilization of mineral deposits, pipe and boiler scale, films on surfaces, constituents of ores, and similar insoluble materials. Chelates having suitable solubilities can be designed to concentrate a metal into a particular phase by extraction from water into an organic solvent, by binding to a liquid but water-insoluble chelant, by precipitation of the chelate as a solid phase, or by ion exchange onto an insoluble, solid, chelating resin. Color and color fastness in some dyeing processes depend on the properties of chelates. The phthalocyanine [574-93-6] pigments (qv) are intensely colored, insoluble chelates. The color of chelates is the basis for many analytical procedures. Catalytic effects may result from a chelate, or chelation of the reactant may itself be part of the mechanism of catalysis by a metal. In biological systems the properties of some enzymes and vitamins (qv) involve chelation, and the activities of chlorophyll and hemoglobin are associated with their chelate structures.

In photography, specially designed chelates suppress or release metal ions to start or stop reactions at appropriate stages in processing sequences, sensitize or desensitize substances to radiation, function in optical and multiplex recording systems, and replace the less environmentally suitable ferricyanide for bleaching (33). Chelates have been used in the preparation of superconducting compounds (34) and as cross-linking agents in fracturing fluids and plugging gels for subterranean formations (35).

Catalysis. In catalysis (qv), the importance of coordination between ligands and metals has long been recognized. The special properties of chelating ligands are especially evident in asymmetric syntheses catalyzed by chelates of an asymmetric ligand, such as in the homogeneous hydrogenation of double-bond functions by a chelate of cobalt and the chiral ligand quinine [130-95-0], $C_{20}H_{24}N_2O_2$ (36). In another application, a cobalt chelate is used as an oxygen carrier in the sweetening of gasoline by oxidation of mercaptans.

Chelation is a feature of much research on the development and mechanism of action of catalysts. For example, enzyme chemistry is aided by the study of reactions of simpler chelates that are models of enzyme reactions. Certain enzymes, coenzymes, and vitamins possess chelate structures that must be involved in the mechanism of their action. The activation of many enzymes by metal ions most likely involves chelation, probably bridging the enzyme and substrate through the metal atom. Enzyme inhibition may often result from the formation by the inhibitor of a chelate with a greater stability constant than that of the substrate or the enzyme for a necessary metal ion.

Many reactions catalyzed by the addition of simple metal ions involve chelation of the metal. The familiar autocatalysis of the oxidation of oxalate by permanganate results from the chelation of the oxalate and Mn(III) from the permanganate. Oxidation of ascorbic acid [50-81-7], $C_6H_8O_6$, is catalyzed by copper (12). The stabilization of preparations containing ascorbic acid by the addition of a chelant appears to be negative catalysis of the oxidation but results from the sequestration of the copper. Many such inhibitions are the result of sequestration. Catalysis by chelation of metal ions with a reactant is usually accomplished by polarization of the molecule, facilitation of electron transfer by the metal, or orientation of reactants.

Chelation itself is sometimes useful in directing the course of synthesis. This is called the template effect (37). The presence of a suitable metal ion facilitates the preparation of the crown ethers, porphyrins, and similar heteroatom macrocyclic compounds. Coordination of the heteroatoms about the metal orients the end groups of the reactants for ring closure. The product is the chelate from which the metal may be removed by a suitable method. In other catalytic effects, reactive centers may be brought into close proximity, charge or bond strain effects may be created, or electron transfers may be made possible.

The crown ethers and cryptates are able to complex the alkali metals very strongly (38). Applications of these agents depend on the appreciable solubility of the chelates in a wide range of solvents and the increase in activity of the co-anion in nonaqueous systems. For example, potassium hydroxide or permanganate can be solubilized in benzene [71-43-2] by dicyclohexano-[18]-crown-6 [16069-36-6]. In nonpolar solvents the anions are neither extensively solvated nor strongly paired with the complexed cation, and they behave as naked or bare anions with enhanced activity. Small amounts of the macrocyclic compounds can serve as phase-transfer agents, and they may be more effective than tetrabutylammonium ion for the purpose. The cost of these macrocyclic agents limits industrial use.

Precipitation and Extraction. The processes of extraction and precipitation comprise transferring the metal into another phase. If the ligand charges neutralize those of the metal ion, the complex becomes a neutral molecule. As the size of the hydrophobic part of the ligands increases, the neutral chelates become less soluble in water and precipitate when enough chelate is present to exceed the solubility. Some ligands precipitate certain metals essentially quantitatively. These materials are used for analytical methods and for recovery of metals from ores or from waste streams. Oxine (8-hydroxyquinoline) is a well-known precipitating agent. Selective and successive precipitations are used in the separation and recovery of the rare-earth elements. Passivation of metals by many organic corrosion inhibitors may involve the formation of an insoluble chelate film with the oxide on the surface or with the metal itself (39) (see CORROSION AND CORROSION INHIBITORS).

A special kind of transfer of metal ions to a solid phase is found in chelating resins, which are similar to ordinary cation-exchange resins except that they have chelating groups in place of the salt-forming moieties. The behavior of the two kinds of resins is similar except that the special effects of the chelation equilibria must be considered. An important use of chelating resins is for the preconcentration of metal ions from such media as seawater, body fluids, and geological materials in which concentration is exceedingly small, so that these ions may be detected or determined analytically (40). Chelating resins may be used functionally in process streams (41).

If a neutral chelate formed from a ligand such as acetylacetone is sufficiently soluble in water not to precipitate, it may still be extracted into an immiscible solvent and thus separated from the other constituents of the water phase. Metal recovery processes (see MINERAL RECOVERY AND PROCESSING), such as from dilute leach dump liquors, and analytical procedures are based on this phase-transfer process, as with precipitation. Solvent extraction theory and many separation systems have been reviewed (42).

Displacement. In many of the applications of chelating agents, the overall effect appears to be a displacement reaction, although the mechanism probably comprises dissociations and recombinations. The basis for many analytical titrations is the displacement of hydrogen ions by a metal, and the displacement of metal by hydrogen ions or other metal ions is a step in metal recovery processes. Some analytical pM indicators function by changing color as one chelant is displaced from its metal by another.

The pH effect in chelation is utilized to liberate metals from their chelates that have participated in another stage of a process, so that the metal or chelant or both can be separately recovered. Hydrogen ion at low pH displaces copper, eg, which is recovered from the acid bath by electrolysis while the hydrogen form of the chelant is recycled (43). Precipitation of the displaced metal by anions such as oxalate as the pH is lowered (Fig. 4) is utilized in separations of rare earths. Metals can also be displaced as insoluble salts or hydroxides in high pH domains where the pM that can be maintained by the chelate is less than that allowed by the insoluble species (Fig. 3).

Rare earths have been separated by elution from ion-exchange resins with chelates of iron, manganese, and cadmium. In another separation, a band of rare earths on an ion-exchange resin was eluted with a chelant and the eluate was passed over an ion-exchange bed loaded with copper. The copper displaced the rare-earth metals that deposited on the second bed. In a solution mining process, a leach solution of $Na_2CaEDTA$ and sodium bicarbonate exchanges Ca for Cu, and the copper is then displaced by lime and the leach solution is regenerated (28). In using chelated chromium in leather tanning, the chromium is captured from the chelant by the collagen in the hide.

The calcium form of EDTA instead of free EDTA is used in many food preparations to stabilize against such deleterious effects as rancidity, loss of ascorbic acid, loss of flavor, development of cloudiness, and discoloration. The causative metal ions are sequestered by displacing calcium from the chelate, and possible problems, such as depletion of body calcium from ingestion of any excess of the free chelant, had it been used, are avoided.

Medical Uses. A significant usage of chelation is in the reduction of metal ion concentrations to such a level that the properties may be considered to be negligible, as in the treatment of lead poisoning. However, the nuclear properties of metals may retain their full effect under these conditions, eg, in nuclear magnetic resonance or radiation imaging and in localizing radioactivity.

In the treatment of poisoning by lead or other metal ions, higher concentrations of chelant can be safely obtained in humans by administering Na₂CaEDTA rather than Na₄EDTA. The metal ion is bound by displacing small amounts of Ca²⁺ that the body can tolerate. Use of Na₄EDTA would result in calcium chelation and thus serious depletion of calcium in the body fluids (44). Removal of iron in Cooley's anemia is accomplished by using chelants that are relatively specific for iron (45).

Bifunctional chelating agents are capable of being covalently attached to an antibody having specificity for cancer or tumor cell epitopes or antigens (see CHEMOTHERAPEUTICS, ANTICANCER). Radioactive metal complexes of such antibody–chelant conjugates are useful in diagnostic, eg, imaging, and therapeutic (irradiation) applications as a means of delivering the radioactive metal to a cancer or tumor cell or to a specific tissue or location (46). Technetium-99m chelates are the most widely used agents in nuclear medicine for diagnostic imaging of the brain, liver, kidneys, and skeleton. Chelants commonly used include diethylene-triaminepentaacetic acid [67-43-6], 1-hydroxyethylidene-1,1-diphosphonic acid [2809-21-4], and glucoheptonate (47). Organophosphonic acid chelates of the radioactive isotopes samarium-153 and thenium-186 have shown promise in bone cancer therapy (48). Gadolinium(III) complexes have been used to enhance the nuclear magnetic resonance images of cerebral tumors (49).

Environmental, Health, and Safety

The primary industrial chelating agents are essentially environmentally benign and nontoxic under the conditions incidental to normal handling and use. With these, eye irritation is mainly a function of the acidity or alkalinity of the form of the product and its solubility. However, use of nitrilotriacetic acid (NTA) is regulated in some jurisdictions. In medical uses the effects of the chelating agents on metal ion balances in the body tissues must be accommodated. Some of the commercial compounds used in smaller amounts as chelants, such as oxalic acid [144-62-7], are toxic, however. The hazards of using any chelant should be determined prior to use.

Solutions of iron chelates can be used to remove hydrogen sulfide and oxides of sulfur and nitrogen in industrial gas scrubbing processes (41,50,51) before flue gases are released to the atmosphere.

Economic Aspects

Production and price estimates for the principal industrial chelating agents are given in Table 5. The list is dominated by sodium tripolyphosphate (STPP), but only a small fraction of this product is used in chelation applications (see PHOSPHORIC ACID AND THE PHOSPHATES). Its primary chelating use is in water treatment and cleaning formulations. Most of the citric acid (qv) is also consumed in nonchelant applications in the food and beverage industry. Citric acid is used for its chelating properties mainly in cleaning applications where STPP is not suitable.

Table 5. United States Production of Industrial Chelating Agents^a

Agent	Production, 10 ³ t yr ^b	Price range ^c \$ /kg	Producers ^d
STPP	277 (241)	0.66–0.88	F, Mon, Oc, Ol, R-P
citric acid	143 (147)	0.88–1.98	HRC, Pfi
aminopolycarboxylic acids	104 (66)		C-G, D, WRG
30–40 ^o solutions		0.66–1.98	
powders crystals		3.31–7.94	
gluconic acid	7 (11)	0.77–1.32	A, B, Pfa, Pfi, PMP
glucoheptonic acid ^e	9 (8)	0.44–1.54	B, Pfa
organophosphonates	12 (16)	1.54–2.42	Ma, Mon

^a Estimated for 1990; includes all forms of the compounds (50).

^b Thousands of metric tons consumed per year given in parentheses.

^c Depends on form of compound and size of shipment.

^d F = FMC Corp.; Mon = Monsanto Co.; Oc = Occidental Petroleum Corp.; Ol = Olin Corp.; R-P = Rhone-Poulenc Inc.; HRC = Haarmann & Reimer Corp. (subsidiary of Bayer USA, Inc.); Pfi = Pfizer Inc.; C-G = Ciba-Geigy Corp.; D = The Dow Chemical Company; WRG = W.R. Grace & Co.; A = Akzo America Inc.; B = Belzak Corp.; Pfa = Pfanstiehl Laboratories, Inc.; PMP = PMP Fermentation Products, Inc.; Ma = Mayo Chemical Co.

^e Glucoheptonic acid [23351-51-1], C₇H₁₄O₈.

The aminopolycarboxylic acids are used principally as chelating agents, and a large proportion is used in water treatment and cleaning formulations. The data of Table 5 include nitrilotriacetic acid (NTA), most of which was exported.

Gluconates and glucoheptonates are largely interchangeable except in foods where the heptonates are prohibited. These compounds chelate polyvalent metals in strongly alkaline solution and are used in many ways, including metal cleaning, bottle washing, food service cleaning applications, electroplating, derusting, aluminum etching, and in concrete. Alkaline gluconate solutions dissolve ferric oxide.

Organophosphonates are similar to polyphosphates in chelation properties, but they are stable to hydrolysis and replace the phosphates where persistence in aqueous solution is necessary. They are used as scale and corrosion inhibitors (52) where they function via the threshold effect, a mechanism requiring far less than the stoichiometric amounts for chelation of the detrimental ions present. Threshold inhibition in cooling water treatment is the largest market for organophosphonates, but there is a wide variety of other uses (50).

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CHEMICAL CLEANING.

See METAL SURFACE TREATMENTS.

CHEMICAL GROUTS.

See SOIL STABILIZATION.

CHEMICAL VAPOR DEPOSITION.

See EELECTRONIC MATERIALS; FILM DEPOSITION TECHNIQUES; THIN FILMS.

CHEMICALS IN WAR

Chemicals used in war fit into five categories: flame agents, incendiaries, smokes and obscurants, riot control agents, and toxic agents. Flame and incendiary agents are used to harass and inflict casualties, and to destroy structures and matériel. Smokes and obscurants are employed for screening, signaling, and target marking, in both offensive and defensive applications. Riot control agents are nonlethal tear agents most effective against unprotected personnel. Toxic chemical agents, used to achieve military objectives by producing casualties and discouraging enemy troops from certain areas of the battlefield (terrain denial), may be incapacitating or lethal.

Chemical warfare, a term used since 1917, is of vital interest not only to the world powers, but also to many developing countries. The relative simplicity of production and ease with which existing pesticide or other chemical plants can be converted to a weapons facility, make chemical weapons a continuing threat. Iraq and Libya, each of which possesses chemical weapon production facilities, have been known to use chemicals in war during the latter part of the 20th century. Chemical weapons are not, as of this writing, banned. Thus whether employed or not, these materials exist as a potential weapon in any conflict. Toxic chemical agents may be defined as chemical substances in gaseous, liquid, or solid state intended to produce casualty effects ranging from harassment through varying degrees of incapacitation to death. A few such agents are true gases but most are solids or liquids that are converted in use into a gaseous state or disseminated as aerosols (qv). For contamination of terrain the agent can also be disseminated in bulk form with or without additives to modify physical properties.

The use of chemical agents and weapons in war is commonly thought to be a modern military technique. However, several historic uses are reported (1) including the contamination of drinking water and an attack against ships with earthen pots filled with live serpents, both before the birth of Christ. An excellent survey of the many factors involved in the use of toxic chemicals in war, including historical background, legal aspects, attempts at international agreement, and reasons why toxic chemicals were not employed in World War II or the Korean Conflict, is available (2).

The modern history of the military use of toxic chemical agents (1,3–5) dates from the first full-scale (chlorine) gas attack on April 22, 1915, near Ypres, Belgium in World War I. There were a few reports of the limited use of toxic chemicals since that time. The Italians employed mustard, a blister agent, during the Ethiopian war in 1935 and 1936; the Japanese used toxic chemicals in a number of small-scale engagements in the early years of their war with China; and Iraq purportedly employed both mustard and nerve gases in the 1980s.

Since World War I, many thousands of chemical compounds have been studied, but the only new and potent class of toxic agents found were those known as the nerve agents: tabun, sarin, and soman (5–7). In the United States these are called the G-agents. A less volatile group is the V-agents. These compounds are a great deal more toxic than either mustard or chlorine and are capable of being disseminated by munition systems including bombs, artillery rounds, rockets, grenades, missiles, and aerial spray (6,8).

Toxic chemical munitions have unique characteristics in comparison to other weapons systems, reaching personnel both widely dispersed and concentrated in fortifications, ie, gases and aerosols are not bound by corners. These materials can penetrate crevices reaching personnel physically protected from high explosives. In addition, toxic chemicals are minimum-destruction weapons as regards matériel (5).

Toxic chemical agents produce a variety of physiological effects depending on the nature of the agent. These effects, which range from death to mild incapacitation used for riot control (6), include blistering, choking, blood poisoning, lacrimation, nerve poisoning, laxation, and various forms of mental and physical disorganization.

Some of the criteria used in the selection of a suitable agent are effectiveness in extremely small concentrations; time to onset of action; effectiveness through various routes of entry into the body, such as the respiratory tract, eyes, and skin; stability in long-term storage; and ease of dissemination in feasible munitions.

Lethal Agents and Incapacitants

Research on chemical agents after World War I led to the elimination of all but a handful of chemicals as being of practical battlefield significance. At the time of World War II the only chemicals considered to be of practical significance included the mustard gases and phosgene.

Discovery of nerve agents in Germany led to the availability of a class of compounds at least one order of magnitude more lethal than previously known where death might occur in a matter of minutes instead of hours.

Mustard and Related Vesicants. Mustard, bis(2-chloroethyl) sulfide [505-60-2] (Chemical Agent Symbol HD), Cl(CH₂)₂S(CH₂)₂Cl, is a colorless, oily liquid when pure. Most samples have a characteristic garliclike odor. It is primarily a vesicant: blisters are formed by either liquid or vapor contact. Mustard also attacks the eyes and lungs and is a systemic poison, so that protection of the entire body must be provided. It is insidious in its action; there is no pain at the time of exposure, and symptoms usually do not appear until several hours after exposure.

Its primary military application is to restrict the use of terrain or lower the mobility of opposing personnel in a contaminated area. It is volatile enough to be effective as a vapor in warm weather. Relatively modest expenditures of munitions yield severely incapacitating vapor dosages within less than an hour (6).

In the period following World War I and during World War II, a wide variety of sulfur analogues of mustard were investigated and many potent vesicants were discovered. Each had two 2-chloroethyl groups attached to a sulfur atom. Examples of such compounds are

1,2-bis(2-chloroethylthio)ethane [3563-36-8] (Chemical Agent Symbol Q), $\text{Cl}(\text{CH}_2)_2\text{S}(\text{CH}_2)_2\text{S}(\text{CH}_2)_2\text{Cl}$; and bis(2-chloroethylthioethyl) ether [63918-89-8] (T), $\text{Cl}(\text{CH}_2)_2\text{S}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{S}(\text{CH}_2)_2\text{Cl}$. It is noteworthy that each 2-chloroethyl group is associated with a separate sulfur atom, not with the same one as for mustard. Both Q and T are more vesicant than mustard, but neither is as volatile. For that reason neither is as effective by the vapor route. One disadvantage of sulfur mustard, however, is that it freezes at ca 10°C, so that solidification in airplane spray tanks presents a serious problem.

The procedure by which mustard is manufactured can be modified to yield either a mixture of mustard and Q (HQ) or a mixture of mustard and T (HT). These mixtures have several advantages over mustard alone, unless the agent is used only for vapor effects. HQ and HT are both more toxic, more vesicant, more persistent, and have lower melting points than mustard alone.

In 1935 nitrogen analogues of sulfur mustards were first synthesized and found to have marked vesicant action (9). These are tertiary amines containing at least two 2-chloroethyl groups, $\text{RN}(\text{CH}_2\text{CH}_2\text{Cl})_2$. The most important of these compounds were tris(2-chloroethyl)amine [555-77-1] (Chemical Agent Symbol HN3), $\text{N}(\text{CH}_2\text{CH}_2\text{Cl})_3$; *N*-methyl-2,2'-dichlorodiethylamine [51-75-2] (HN2), $\text{CH}_3\text{N}(\text{CH}_2\text{CH}_2\text{Cl})_2$; and 2,2'-dichlorotriethylamine [538-07-8] (HN1), $\text{CH}_3\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{Cl})_2$. The nitrogen mustards are colorless when pure but turn yellow to amber in storage. These materials have faint odors varying from fishy or soft-soaplike to practically odorless, and they act on the body in a manner similar to sulfur mustard.

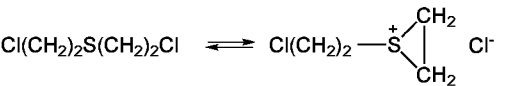
Properties. The physical properties of the mustards are summarized in Table 1. The sulfur mustards are only slightly soluble in water, whereas the nitrogen mustards are slightly soluble at neutral pH, but form water-soluble salts under acid conditions. Both sulfur and nitrogen mustards are extremely soluble in most organic solvents.

Table 1. Properties of Mustard Gases

Property	HD	Q	T	HN1	HN2	HN3
mol wt	159.08	219.08	263.25	170.08	156.07	204.54
bp, °C ^a	80 ^{0 7}		120 ^{0 003}	85 ^{1 3}	87 ^{2 4}	144 ^{2 0}
mp, °C	14.5	56	10	34	60	4
density at 25°C, g mL	1.2682		1.24	1.086	1.118	1.2347
volatility at 25°C, mg m ³	925	0.4	2.8	2.29	3.581	0.120

^a Pressure in kPa at which boiling point was determined is given as a superscript. To convert kPa to mm Hg, multiply by 7.5.

Although sulfur and nitrogen mustards have limited solubility in water at neutral pH, the small quantity that dissolves is extremely reactive. The reaction proceeds via a cyclic sulfonium or imonium intermediate



This intermediate attacks compounds containing a variety of functional groups, such as primary, secondary, and tertiary amino nitrogen atoms, carboxyl groups, and sulfhydryl groups (10).

With nitrogen mustards, the imonium ion, which apparently forms even in the absence of any solvent, readily attacks another molecule to form a dimer. For this reason, the nitrogen mustards are less stable than sulfur mustards in long-term storage.

An excellent reagent for detection and quantitative estimation of the mustards is *p*-nitrobenzylpyridine (11). On treatment of the reaction product with alkali a blue color appears, which detects as little as 0.1 µg of mustard.

The mustards readily alkylate inorganic thiosulfates to form Bunte salt anions (12,13). For sulfur mustard, the product is $\text{Cl}(\text{CH}_2)_2\text{S}(\text{CH}_2)_2\text{SSO}_3^-$. Phosphates react in a similar manner and the product isolated from sulfur mustard is $\text{Cl}(\text{CH}_2)_2\text{S}(\text{CH}_2)_2\text{OPO}_3^{2-}$.

Sulfur mustard reacts rapidly with chlorine or with bleach, and this reaction is a suitable means of decontamination. Nitrogen mustards, however, chlorinate extremely slowly; thus chlorination is not suitable for their decontamination. The formation of water-soluble salts, such as by neutralization with sodium bisulfate, is the usual method for nitrogen mustard removal from contaminated surfaces. The mustard salts are much less vesicant than the corresponding free bases.

The mustards can be oxidized by such oxidizing agents as hydrogen peroxide or potassium bichromate in sulfuric acid. Oxidation occurs at the sulfur atom of sulfur mustard and at the nitrogen atom of nitrogen mustard. The product formed on strong oxidation of sulfur mustard, bis(2-chloroethyl)sulfone, [471-03-4], $(\text{ClCH}_2\text{CH}_2)_2\text{SO}_2$, exhibits vesicant properties.

Physiological Effects. The sulfur and nitrogen mustards act first as cell irritants and finally as a cell poison on all tissue surfaces contacted. The first symptoms usually appear in 4–6 h (4). The higher the concentration, the shorter the interval of time between the exposure to the agent and the first symptoms. Local action of the mustards results in conjunctivitis (inflammation of the eyes); erythema (redness of the skin), which may be followed by blistering or ulceration; and an inflammatory reaction of the nose, throat, trachea, bronchi, and lung tissue. Injuries produced by mustard heal much more slowly and are much more liable to infection than burns of similar intensity produced by physical means or by other chemicals.

The rate of detoxification is slow, and the effects of even very small repeated exposures are cumulative or more than cumulative owing to sensitization.

Uses The nitrogen mustards are used clinically in the treatment of certain neoplasms (14). They have been used in treatment of Hodgkin's disease, lymphosarcoma, and leukemia (see CHEMOTHERAPEUTICS, ANTICANCER).

Nerve Agents. This term refers to two groups of highly toxic chemical compounds that generally are organic esters of substituted phosphoric acid (5–7). The nerve agents inhibit cholinesterase enzymes and thus come within the category of anticholinesterase agents (see ENZYME INHIBITORS). The three most active G-agents are tabun, ethyl phosphorodimethylamidocyanide [77-81-6] (Chemical Agent Symbol GA), $(\text{CH}_3)_2\text{NPOCNOC}_2\text{H}_5$; sarin, isopropylmethylphosphonofluoridate [107-44-8] (GB), $\text{CH}_3\text{POFOCH}(\text{CH}_3)_2$; and soman, pinacolyl methyl-phosphonofluoridate [96-64-0] (GD), $\text{CH}_3\text{POFOCHOCH}_2\text{C}(\text{CH}_3)_3$.

The G-agent liquids under ordinary atmospheric conditions have sufficiently high volatility to permit dissemination in vapor form. They are generally colorless, odorless or nearly so, and are readily absorbable through not only the lungs and eyes but also the skin and intestinal tract without producing any irritation or other sensation on the part of the exposed individual. These agents are sufficiently potent so that even a brief exposure may be fatal. Death may occur in 1–10 min, or be delayed for 1–2 h depending on the concentration of the agent.

Another class of nerve agents, discovered after World War II, is the V-agents. These materials are generally colorless and odorless liquids that do not evaporate rapidly at normal temperatures. In liquid or aerosol form, V-agents affect the body in a manner similar to the G-agents. The advantage is that V-agents produce casualties when absorbed through the skin in concentrations much lower than those required by the G-agents. Aerosolized V-agents are also quite lethal by inhalation.

Properties. Some physical properties of nerve agents are given in Table 2. The G-agents, miscible in both polar and nonpolar solvents, hydrolyze slowly in water at neutral or slightly acid pH and more rapidly under strong acid or alkaline conditions. The hydrolysis products are considerably less toxic than the original agent.

Table 2. Properties of Nerve Agents

Property	GA	GB	GD	VX ^a
formula wt	162.13	140.10	182.18	267.38
bp, °C	246	147	167	298
mp, °C	50	56	unknown	below 51
density at 25°C, g mL	1.073	1.0887	1.0222	1.0083
volatility at 25°C, mg m ³	610	21,900	3,060	10.5

^a VX [50782-69-9], C₁₁H₂ NO₂PS, is a phosphonothioic acid ester.

GB is unstable in the presence of water. Maximum stability in aqueous solutions occurs from pH 4.0–6.5 with the hydrolysis rate increasing as the pH increases. The half-life in distilled water at 25°C is ca 36 h, but hydrolysis is accelerated in the presence of acids or bases. Because bases are far more effective in this respect than acids, caustic solutions are useful for decontamination.

GB decomposes thermally to form a variety of phosphorus-containing products as well as propylene. The rate of decomposition increases with increase in temperature and in the presence of acids. At the boiling point of GB, under atmospheric conditions, decomposition is fairly rapid.

GB and other G-agents react with perhydryl ions at pH 9–10 to form a perphosphonate ion, CH₃P(O)(OC₂H₅)OO⁻, which has a sufficiently high redox potential to oxidize indole or *o*-dianisidine to produce colored products. This reaction is thus useful as a method of detection, and less than 1 µg of GB can be detected in this manner (15).

Another useful reagent for detection and estimation of G-agents is diisonitrosoacetone (16). A magenta color is produced with 1 µg of GB at pH 8.5. Coupling agents, such as *p*-phenylenediamine, increase the reaction rate.

Physiological Effects. Inhalation of G-agent vapor at realizable field concentrations is immediately incapacitating. The symptoms in normal order of appearance are runny nose; tightness of chest; dimming of vision and pinpointing of the eye pupils (miosis); drooling and excessive sweating; nausea and vomiting; cramps and involuntary defecation or urination; twitching, jerking, and staggering; and headache, confusion, drowsiness, coma, and convulsion. These symptoms are followed by cessation of breathing and death.

Although GB is also effective by penetration through the skin, the dose required to produce toxic effects by this route is high. Thus a person wearing skin covering and a gas-mask is reasonably well protected.

VX (6,7) is estimated to be about three times as potent a respiratory agent as sarin (GB) but about a hundred times as potent as a percutaneous agent.

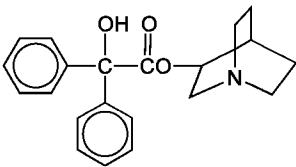
Binary Munitions. Binary munitions contain two nonlethal components that are mixed during flight to form a nerve agent. Each component is manufactured separately, remaining in its own container until the munition components are assembled just prior to use. Mixing and subsequent agent formation occurs after firing or launch of the munition. In addition to greatly reduced storage and handling hazards, the binary components can be manufactured in ordinary chemical facilities, which need not be equipped with the stringent safety and environmental controls required for the older nerve agent munitions. The binary technology also overcomes the long-term storage problems associated with the unitary nerve agents.

Other Lethal Agents. There are a number of substances, many found in nature, which are known to be more toxic than nerve agents (6). None has been weaponized. Examples of these toxic natural products include shellfish poison, isolated from toxic clams; puffer fish poison, isolated from the viscera of the puffer fish; the active principle of curare; "heart poisons" of the digitalis type; the active principle of the sea cucumber; active principles of snake venom; and the protein ricin, obtained from castor beans (See CASTOR OIL).

Incapacitants. Incapacitating agents, or incapacitants, are just what the name implies. In wartime, soldiers and civilians must be physiologically, physically, and mentally able to perform their jobs. Thus, an agent rendering an individual incapable of job performance may be classified as an incapacitating agent (6,7).

Incapacitants are most suitable for consideration in limited warfare situations, eg, when enemy troops are intermingled with a friendly population, or in a city that is a key military objective. The purpose is to capture the enemy without killing the civilians. Incapacitating agents should produce no permanent after-effects and allow for complete recovery.

Agent BZ, 3-quinuclidinyl benzilate [6581-06-2], C₂₁H₂₃NO₃, is a typical incapacitant. BZ is one of a group of substances, many of them glycolate esters, sometimes known as atropinemimetics. Their action on the central and peripheral nervous systems resembles that of atropine [51-55-8], C₁₇H₂₃NO₃. The effects of BZ are those of an anticholinergic psychotomimetic drug (6). These effects follow about a half hour after exposure to BZ aerosol, reach a peak in four to eight hours, and may then take up to four days to pass. Effects include disorientation with visual and auditory hallucinations. The agent disturbs the higher integrative functions of memory, problem solving, attention, and comprehension. There is a gradual return to normalcy.



BZ

By U.S. Army criteria, incapacitation agents do not include (7): (1) lethal agents that are incapacitating at sublethal doses, such as nerve agents; (2) substances that cause permanent or long-lasting injury, such as blister agents, choking agents, and those causing eye injury; (3) drugs that exert marked effects on the central nervous system, such as barbiturates, belladonna alkaloids (qv), tranquilizers, and many of the hallucinogens. These drugs are logistically infeasible for large-scale use because of the high doses required (see HYPNOTICS, SEDATIVES, AND ANTICONVULSANTS; NEUROREGULATORS; PSYCHOPHARMACOLOGICAL AGENTS); (4) agents of temporary effectiveness that produce reflex responses interfering with performance of duty. These include skin and eye irritants causing pain or itching (vesicants or urticants), vomiting- or cough-producing compounds (sternutators), and tear compounds (lacrimators); and (5) agents that disrupt basic life-sustaining systems of the body and thus prevent physical activity. These include agents that lower blood pressure, paralyzing agents such as curare, fever-producing agents, and blood poisons. Such agents almost invariably have a narrow margin of safety between the effective and possibly lethal doses, and the basic purpose of an incapacitating agent is to reduce military effectiveness without endangering life.

Use. Owing to inherent physical characteristics, chemical agents can be adapted to a variety of munitions, including grenades, mines, artillery shells, bombs, bomblets, spray tanks, rockets, and missiles. Tactically, chemical agents have defensive and offensive capabilities in limited or general wars. Toxic chemical agents may be used alone or in conjunction with other types of weapons. Chemical weapons do not destroy matériel but allow physical preservation of industrial complexes and other facilities. Incapacitating agents may also be used to preserve life and avoid permanent injury.

The use of chemical agents in battle imposes a significant burden on troops because of the cumbersome nature of the protective clothing and the attendant heat load in hot climate situations. This factor alone imposes a burden on potential target personnel, lowering their effectiveness. U.S. troops in the 1991 Mideast war Desert Storm were provided with protective gear that did not deter them with regard to the outcome of the action.

Irritants

Irritant compounds such as the lacrimators and sternutators used in World War I are traditional examples of harassing agents, the effects of which are reversible and briefly incapacitating. Riot control agent CS, a modern irritant compound (6,7), causes physiological effects that include extreme burning of the eyes, accompanied by a copious flow of tears; coughing; difficulty in breathing; chest tightness; involuntary closing of the eyes; stinging sensation of moist skin; runny nose; and dizziness or "swimming" of the head. Heavy concentrations also cause nausea and vomiting.

The effects of agent CS are immediate, even in extremely low concentrations. The median concentration for respiratory effects is 12–20 mg m⁻³; for eye effects it is 1–5 mg m⁻³. The onset of maximum effects is 20–60 s, and the duration is 5–10 min after the individual has been removed to fresh air.

A water-soluble white crystalline solid, CS is disseminated as a spray, as a cloud of dust or powder, or as an aerosol generated thermally from pyrotechnic compositions. The formulation designated CS1 is CS mixed with an anti-agglomerant; when dusted on the ground, it may remain active for as long as five days. CS2 formulated from CS1 and a silicone water repellent, may persist for as long as 45 days (6).

The principal uses of CS are in riot control and training; it has limited tactical use in defensive military modes (17).

Flame

In the modern weapons arsenal flame agents are defined as various hydrocarbons, blends of hydrocarbons, and other readily flammable liquids, usually thickened with additives, that are easily ignited and can be projected to military targets (7). Although flame agents may be employed against buildings and other flammable targets, their primary role is against personnel in hardened structures or emplacements. In the United States, the principal application of flame agents is now in flame throwers and flame projectors, including flame rockets. The firebomb is becoming obsolete. The replacement for the portable flame thrower is the multishot flame rocket, which delivers an encapsulated flame warhead directly to the target from a significantly great and safe range. The large-caliber flame rounds could become all-weather, highly aimable replacements for the obsolete air-deliverable fire bombs and the mechanized flame throwers.

Flame Throwers and Projectors. One advance in flame throwers since World War II was a mechanized flame thrower kit for a variety of armored vehicles other than the main battle tank. The multishot, lightweight, shoulder-fired, four-tube flame system capable of firing one to four flame rounds semiautomatically is replacing the portable flame thrower. Indeed the mechanized flame thrower is expected to become obsolete because of the family of large-caliber flame rounds.

The U.S. Army's M202 M74 flame system is a shoulder-fired, four-tube launcher equipped with front and rear hinged protective covers. A folding sight and trigger handle assembly provide compact carrying and storage capabilities. An adjustable sling is used to carry the launcher over the shoulder. The rocket system is aimed and fired from the right shoulder from the standing, kneeling, sitting, or prone position. Ammunition for the launcher is provided in rocket clips preloaded with four rockets that slip-fit into the four launcher tubes. The user can fire from one to four rockets semiautomatically at a rate of one per second; the launcher can be reloaded with a new clip repeatedly. The flame agent payload is thickened pyrophoric agent TPA, a polyisobutylene-thickened metal alkyl formulation (18).

Fire Bombs. After World War II the fire bomb became a standard item of military equipment. A cigar-shaped, thin-cased tank similar in appearance to the aircraft fuel tank from which it evolved, the typical fire bomb consisted of the basic tank, two igniters, two fuses, an arming wire, and the flame agent payload. Most fighter and fighter-bomber aircraft carried two, one under each wing. Ideal delivery was at low altitude, almost level flight, with the fire bomb impacting along the aircraft flight path and producing a rolling wall of flame covering an area ca 35 m wide and 100 m in length. The initial fireball, a direct function of flame agent quality, burned for about 10 s with intense heat. The dispersed particles could burn for up to 10 min but at greatly reduced intensity.

Upon the advent of high performance jet-powered aircraft, the fire bomb became obsolete. When delivered at speeds approaching Mach one (345 m s), the design characteristics were often grossly exceeded and many units broke up or functioned while still on the aircraft. Delivery from high altitude created craters and deposited most of the flame agent payload in those craters.

Studies of fire bomb modifications and the corresponding flame agent payloads were terminated once the controlled fireball damage mechanism was developed. In field firings it was shown that large-caliber flame rounds could produce equivalent effects. The rolling wall of reacting flame could be generated, accompanied by a highly aimable, all-weather flame system capable of sustained fire.

Flame Agents. For some time after World War II effort was expended in improvement of naplam-thickened hydrocarbons as the standard flame agents. The problem was the breakdown of the flame agent in the presence of traces of water and the need for peptizers in cold-weather applications. More recently, thickened pyrophoric flame agents (7) have been deployed in the field and as the payload for the U.S. Army's flame rocket system. Advantages of this newer flame agent include: the ability to prepackage warheads and other containers and store them for indefinite periods with no deterioration; and the fact that these pyrophoric flame agents do not require an ignition system to function on the target.

Computer-aided research by army personnel has resulted in development of the controlled fireball damage mechanism for efficient and effective coupling of heat energy to effect maximum thermal damage. Moreover, flame agents may be tailored to each candidate flame system. Optimization of several low viscosity metal-alkyl formulations has also removed the problem of temperature by making these flame agents relatively independent of temperature variations.

Incendiaries

Incendiary agents are designed for use in the planned destruction of buildings, property, and matériel by fire (7). Incendiaries burn with an intense, localized heat. They are very difficult to extinguish and are capable of setting fire to materials that normally do not ignite and burn readily. Although there are tactical applications for incendiary agents and munitions, they have played primarily a strategic role in modern warfare.

Incendiary Requirements. The mechanics of starting fires using incendiary agents involve a source of heat to act as a match to initiate combustion in a larger mass; combustible material to serve as kindling; and fuel. The match and the kindling are provided by the incendiary munition; the target is the fuel. All incendiary munitions, except for those containing materials that are spontaneously combustible, must have some sort of initiator such as a fuse or an ignition cup. The second element of the incendiary munition, the kindling, is the important factor, and both the amount and the nature of the combustible material in the munition have been the subject of much research and development.

The maximum total heat output of an incendiary agent can be readily calculated and it is obviously desirable to use a filling that has a high heat evolution. The rate of the heat release varies with the agent and depends on: flash, fire, or decomposition temperature; particle size of the agent after ejection from the munition, which controls the surface-to-volume ratio of the agent; and oxidizing agents blended with the combustible material to increase the rate of heat evolution. The incendiary agent must be capable of heating the target or fuel until the ignition temperature, which can vary from 200–400°C, is reached. To be really effective, the incendiary agent must generate at least four times as much heat as is necessary to raise the temperature to this point.

Metal Incendiaries. Metal incendiaries include those of magnesium in various forms, and powdered or granular aluminum mixed with powdered iron(III) oxide. Magnesium is a soft metal which, when raised to its ignition temperature, burns vigorously in air. It is used in either solid or powdered form as an incendiary filling, and in alloyed form as the casing for small incendiary bombs.

Magnesium has an ignition temperature of 623°C and a burning temperature of around 1982°C. The burning temperature is variable; it depends on the rate of heat dissipation, rate of burning, and other factors. Magnesium, burning with a blinding white flame, melts as it burns and the burning liquid metal drops to lower levels, igniting all combustible materials in its path. Burning stops if oxygen is prevented from reaching the metal or if the metal is cooled to a point below its ignition temperature. Whereas magnesium does not have the highest heat of combustion of the metals, none of the other metals have been successfully used as air-combustible incendiaries. Some metals may be alloyed with magnesium without affecting its ignitability. The alloyed metal has the strength to withstand distortion, whereas pure magnesium does not. In massive form, magnesium is difficult to ignite. This problem is overcome by packing a hollow core in a bomb with thermite [8049-32-9]. This results in an easily ignited mixture that supplies its own oxygen and burns at a very high temperature.

Thermite is essentially a mixture of ca 73 wt % powdered iron(III) oxide, Fe₂O₃, and 27 wt % powdered or granular aluminum. The aluminum has a

higher affinity for oxygen than iron, and if a mixture of iron oxide and aluminum powder is raised to the combustion temperature of aluminum, an intense reaction occurs



Under favorable conditions the thermite produces temperatures of about 2200°C, high enough to turn the newly formed metallic iron into a white-hot liquid that acts as a heat reservoir to prolong and spread the heat or igniting action.

The thermate mixture, composed of thermite and various additives, is used in igniter compositions for magnesium bombs. A number of such compositions have been developed. Three of these were Therm-8, Thermate-TH2 (formerly Therm-8-2), and Thermate-TH3 (formerly Therm-64-C). Therm-8 was the precursor of later, improved igniting formulations TH2 differs from Therm-8 in that TH2 contains no sulfur and slightly less thermite. TH3 was found to be superior to the others and thus adopted for use in the incendiary magnesium bomb. The wt % composition of TH3 is thermite, 68.7; barium nitrate, 29.0; sulfur, 2.0; and as a binder, oil, 0.3.

The TH3 core is ignited by the primer, and the burning core then melts and ignites the magnesium alloy body of the bomb. The incendiary action on the target is localized. There is little scattering of the incendiary material.

Oil and Metal Incendiary Mixtures. PT1 is a complex mixture composed of magnesium dust, magnesium oxide, and carbon (qv), along with an adequate amount of petroleum (qv) and asphalt (qv) to form the paste (7). The U.S. developers have adopted the formula: type c paste (goop), 49.0 ± 1.0; IM polymer AE, 3.0 ± 1.0; coarse magnesium, 10.0 ± 1.0; petroleum oil extract, 3.0 ± 0.2; gasoline, 30.0 ± 3.0; and sodium nitrate, 5.0 ± 0.5.

PTV is an improved oil and metal incendiary mixture having the composition: polybutadiene, 5.0 ± 0.1; gasoline, 60.0 ± 1.0; magnesium, 28.0 ± 1.0; sodium nitrate, 6.0 ± 0.1; and *p*-aminophenol, 0.1.

Incendiary bombs containing PT1 or PTV mixtures are easily ignited by nose or tail fuses because they contain many combustible ingredients. These formulations contain both metal and an oxidizer, eg, sodium nitrate; thus condensed phase reaction products are obtained. The resulting heat flux conducted to the target is increased, resulting in greater potential target damage.

Smokes

Military smokes are aerosols (qv) of gaseous, liquid, or particulate matter that are tactically employed to defeat enemy surveillance, target acquisition, and weapons guidance devices. The traditional battlefield applications of smoke are screening and marking. Screening smokes are normally employed to obscure a military objective from enemy observation by creating an aerial blanket, vertical curtain, or ground haze. Signaling smokes are pyrotechnic mixtures that incorporate an organic compound dyed for target marking or for transmitting messages by prearranged color code (see PYROTECHNICS).

Battlefield smoke has a great significance in the countermeasure role. Threat weapons no longer rely simply on optical devices that operate in the visible spectrum. Modern lethal weapons are augmented with sophisticated surveillance, target acquisition, and guidance devices that operate throughout the visible, infrared, and microwave (radar) regions of the electromagnetic spectrum. Accordingly, research and development is concentrated on nonvisual multispectral screening systems designed to defeat modern weaponry such as the antitank guided missile (ATGM), laser-guided munitions, and heat-seeking missiles.

Screening Smokes. Military smoke screens are produced by dispersing either finely-divided solids or minute liquid droplets in air. To be useful, a smoke screen must be sufficiently opaque to provide the desired screening power and long-lasting enough to achieve effective military results. In designing a screen for the modern battlefield, it is necessary to defeat sophisticated surveillance technologies that operate in the near-, mid-, and far-infrared as well as in the millimeter wavelength frequencies. Other factors considered in the evaluation of potential screening agents include cost, ease of dispersion, and efficiency of dispersion. Agents used for screening friendly areas must be as nonirritating as possible.

Both the opacity and persistency of smoke screens are largely dependent on the nature of the individual smoke particles. All present U.S. smoke agents produce aerosols. The principal mechanism of obscuration is the scattering effect. To optimize its effectiveness, the aerosol's particle size should be approximately in the same size range as the wavelength of the light to be screened. Many U.S. smoke agents produce aerosols having particle-size distribution that is log-normal having a mean diameter of about 0.6 μm, allowing maximum effectiveness in the visible and near-infrared wavelength regions. More recently, fine fibers have been used as screens for longer wavelengths and in mixtures or combined usage to screen the entire region of concern.

The obscuring action of visual screening smokes is largely caused by reflection and refraction of light by the individual suspended particles of which the smoke is composed (7). Because this obscuring action occurs to the greatest extent in the absence of light-absorbing particles such as carbon, white smokes have the greatest screening action.

The life persistency of a smoke cloud is determined chiefly by wind and convection currents in the air. Ambient temperature also plays a part in the continuance or disappearance of fog oil smokes. Water vapor in the air has an important role in the formation of most chemically generated smokes, and high relative humidity improves the performance of these smokes. The water vapor not only exerts effects through hydrolysis, but it also assists the growth of hygroscopic (deliquescent) smoke particles to an effective size by a process of hydration. Smoke may be generated by mechanical, thermal, or chemical means, or by a combination of these processes (7).

Types of Screening Smokes. The generation of oil smoke is based on the production of minute oil droplets by purely physical means. The most desirable droplet size is 0.5–1.0 μm. The tiny droplets of oil scatter light rays and produce a smoke that appears to be white, and any individual droplet would be transparent under magnification. These droplets are produced as the vaporized oil passes through the nozzle of a generator and is subsequently cooled by the surrounding air. The air cools the oil vapor so quickly that only very small droplets are able to form. The process thus depends on a high oil temperature followed by quick cooling. Proper selection of the smoke oil ensures that the final smoke cloud is stable, and the life of the cloud is determined almost entirely by meteorological conditions. The smoke generator uses a low viscosity petroleum oil (U.S. Army designation: SGF No. 2 smoke generator fog). SGF corresponds somewhat to an SAE 10 (light) motor oil in viscosity. Below 0°C, a mixture of SGF No. 2 and a paraffin-free kerosene is used.

Another type of smoke mixture, a volatile hygroscopic chloride for thermal generation, has the U.S. Army designation HC, type C. It is composed of ca 6.7 wt % grained aluminum, 46.7 wt % zinc oxide ZnO, and 46.7 wt % hexachloroethane [67-72-1], C₂Cl₆. The ratio of zinc oxide to hexachloroethane is held between 1.04 and 1.00, but the aluminum may be varied slightly to regulate the burning time. Because this mixture is composed of solids, it can be compressed to provide high payloads in small volumes, and it is used as a filling for smoke grenades, smoke pots, and artillery shells. The initial heat needed to start the burning of HC is provided by a starter mixture, typically silicon, potassium nitrate, charcoal, iron oxide, grained aluminum, cellulose nitrate, and acetone. A burning HC mixture produces zinc chloride which, in turn, is volatilized by reaction heat and condenses to form a zinc chloride–water smoke.

A third screening smoke-type is white phosphorus [7723-14-0] (WP), P₄ (see PHOSPHORUS AND THE PHOSPHIDES), which reacts spontaneously with air and water vapor to produce a dense cloud of phosphorus pentoxide [1314-56-3]. An effective screen is obtained as the P₂O₅ hydrolyzes to form droplets of dilute phosphoric acid aerosol. WP produces smoke in great quantity, but it has certain disadvantages. Because WP has such a high heat of combustion, the smoke it produces from bulk-filled munitions has a tendency to rise in pillarlike mass. This behavior too often nullifies the screening effect, particularly in still air. Also, WP is very brittle, and the exploding munitions in which it is used break it into very small particles that burn rapidly.

The disadvantages of WP have been overcome to some degree by absorbing WP into felt wedge submunitions that burn and release smoke at a lower rate and by the development of plasticized white phosphorus (PWP). PWP is produced by melting WP and stirring it into cold water, which results in a slurry of WP granules of ca 0.5 mm diameter. The slurry is mixed with a viscous solution of synthetic rubber, so that the granules are coated with a film of rubber and thus separated from each other. When PWP is dispersed by an exploding munition, it does not break into such small particles; the burning rate is slowed, and the tendency of the smoke to pillar is reduced. WP and PWP are used as fill for grenades, artillery shells, mortar shells, bombs, and rockets.

Developments in several countries have resulted in red phosphorus (RP) as a screening smoke agent having less performance problems. RP is an allotropic form of elemental phosphorus, which is made by heating white phosphorus at high temperatures in the absence of air. RP is less reactive than WP and thus lends itself to the manufacture of presized subunits that can be packaged in artillery and mortar shells. These subunits, which are dispersed as multiple smoke-producing sources, enhance target effectiveness by the rapid formation of a large homogeneous and persistent screen. The pillaring phenomenon is thus minimized. Another advantage of RP is that it does not undergo a change of state at operational temperatures thereby precluding the munition instability problems that sometimes occur with WP, which liquefies above 43°C.

A solution of sulfur trioxide [7446-11-9], SO₃, dissolved in chlorosulfonic acid [7990-94-5], ClSO₃H, has been used as a smoke (U.S. designation FS) but it is not a U.S. standard agent (see CHLOROSULFURIC ACID; SULFURIC ACID AND SULFUR TRIOXIDE). When FS is atomized in air, the sulfur trioxide evaporates from the small droplets and reacts with atmospheric moisture to form sulfuric acid vapor. This vapor condenses into minute droplets that form a dense white cloud. FS produces its effect almost instantaneously upon mechanical atomization into the atmosphere, except at very low temperatures. At such temperatures, the small amount of moisture normally present in the atmosphere, requires that FS be thermally generated with the addition of steam to be effective. FS can be used as a fill for artillery and mortar shells and bombs and can be effectively dispersed from low performance aircraft spray tanks. FS is both corrosive and toxic in the presence of moisture, which imposes limitations on its storage, handling, and use.

Signaling Smokes. Screening smokes also can be adapted for signaling purposes. For example, phosphorus-filled artillery and mortar rounds can be used to mark targets and determine range corrections. However, a good signaling smoke must be clearly distinguished from the smoke incident to battle. The standard signaling smokes, described in Table 3, afford good visibility and unmistakable identity. Unfortunately all colors become gray and indistinguishable at great distances, and even excellent signaling smokes have a maximum effective visual range that varies from approximately 1–3 km, depending on the color intensity of the smoke and the type and size of the munition.

Table 3. Colored Smoke Fillings

Ingredient	CAS Registry number	Molecular formula	Composition, wt %
<i>Red smoke</i>			
dye:			
85% 1- <i>N</i> -methylaminoanthraquinone;	[82-38-2]	C ₁₅ H ₁₁ NO ₂	
15% dextrin	[9004-53-9]		42
sodium bicarbonate	[144-55-8]	NaCHO ₃	19
potassium chlorate	[3811-04-9]	KClO ₃	28
sulfur	[7704-34-9]	S	11
<i>Green smoke</i>			
dye:			
70% 1,4,di- <i>p</i> -toluidinoanthraquinone;	[128-80-3]	C ₂₈ H ₂₂ N ₂ O ₂	
10.5% indanthrene golden yellow;	[128-66-5]	C ₂₄ H ₁₂ O ₂	
19.5% benzanthrone	[82-05-3]	C ₁₇ H ₁₀ O	40.0
sodium bicarbonate			22.6
potassium chlorate			27.0
sulfur			10.4
<i>Yellow smoke</i>			
dye:			
65% benzanthrone;	[82-05-3]	C ₁₇ H ₁₀ O	
35% indanthrene golden yellow	[128-66-5]	C ₂₄ H ₁₂ O ₂	38.5
sodium bicarbonate			33.0
potassium chlorate			20.0
sulfur			8.5
<i>Violet smoke</i>			
dye:			
80% 1,4-diamino-2,3- dihydroanthraquinone;	[83-61-0]	C ₁₄ H ₁₂ N ₂ O ₂	
20% 1- <i>N</i> -methylaminoanthraquinone	[82-38-2]	C ₁₅ H ₁₁ NO ₂	42.0
sodium bicarbonate			18.0
potassium chlorate			28.8
sulfur			11.2
<i>Starter</i>			
potassium nitrate	[7757-79-1]	KNO ₃	37.8
silicon	[7440-21-3]	Si	28.0
charcoal	[7440-44-0]	C	4.2
cellulose nitrate	[9004-70-0]		1.2
acetone	[67-64-1]	C ₃ H O	28.8

Colored signaling smokes are produced by volatilizing and condensing a mixture containing an organic dye. Of the dyes tested by the U.S. Army, the most satisfactory ones are the azo dyes (qv), the azine dyes (qv), the diphenylmethane dyes, and those of anthraquinone (qv) (7) (see DYES AND DYE INTERMEDIATES). The filling for a colored smoke munition is essentially a pyrotechnic mixture of fuel and dye, with a cooling agent sometimes added to prevent excessive decomposition of the dye. The heat produced by the fuel volatilizes the dye, and the dye condenses outside the munition to form the colored smoke. In U.S. munitions, the fuel is made up of a mixture of an oxidizing agent such as potassium chlorate, KClO₃, and a combustible material such as sulfur or sugar. The burning time can be regulated by adjusting the proportions of oxidant and combustible material and by use of coolants such as baking soda. A typical starter mixture is given in Table 3. Colored smoke mixtures are used in hand and rifle grenades and in canisters for use with larger projectiles.

Defense Against Toxic Agents

Defensive measures against toxic agents may be divided into four categories: agent detection and identification, individual and collective protection, decontamination, and medical defense. To these may be added a high degree of training in defensive measures and discipline in using them.

Detection. Many modern toxic chemicals are colorless and odorless; therefore, chemical and physical means must be employed in their detection and identification. Also, because of the extreme toxicity of modern chemical agents, especially the nerve agents, very sensitive and selective detection and identification are necessary. Detection is performed using either manually operated kits or automatic battery-operated detectors. The kits usually include absorbent-containing tubes through which the air is drawn in order to concentrate the sample, or filter disks that are exposed to the air for a certain length of time. Liquid reagents are added before and or after exposure to the sample air, usually resulting in some type of color change as a

consequence of agent exposure.

The automatic detectors can use acetylcholinesterase enzyme-inhibition, ie, wet chemistry, diffusion of ionized air samples through a baffled diffusion cell, electrochemical reactions, or ion mobility spectrometry to detect chemical agents selectively. Typically, air is drawn through a filtered inlet into the detector using a pump; chemical agents and other similar chemicals diffuse across a selective membrane and are then ionized, if necessary, by a radioisotope. Detection of the agent results in a visual or audible alarm at either the detector itself or at a remotely located alarm unit. Infrared-detecting interferometers can be used to detect chemical agent vapor at a distance from the agent cloud.

Individual and Collective Protection. The primary item of individual protection is the protective or gas mask. The U.S. Army standard mask is the M17A2, which has as its basic components a molded rubber facepiece with large cheek pouches that hold filter elements. These elements consist of six sheets of core laminated between two sheets of backing layer. The backing layers are composed of vinyl chloride–vinyl acetate copolymer, cellulose, and glass fibers. The core layers are composed of these same materials plus 75% Whetlerite absorbent, a finely ground activated carbon impregnated by immersion in an ammoniacal solution of silver, copper, chromium, and carbon dioxide, and then dried at temperatures sufficient to expel substantially all ammonia from the granules. Inhalation valves are attached to the filter element caps through the cheek-pouch portions of the mask faceblank. A voicemitter-outlet assembly, incorporating a speech diaphragm and an outlet valve, is attached to the faceblank at the mouth position. Large eyepieces in the faceblank provide a wide field of vision. The M17A2 mask provides complete respiratory protection against all known military toxic chemical agents, but it does not provide protection against some industrial toxics such as ammonia and carbon monoxide.

A newer improved mask developed by the U.S. Army is in production and expected to be fielded in the 1990s. The M40 (Figs. 1 and 2) and M42 chemical-biological masks are to replace the M17A2 and several other specialty masks, making for greater logistical simplicity as well as better respiratory, eye, and face protection against field concentrations of chemical and biological agents. Improvements include an externally mounted NATO standard canister, front and side voicemitters, microphone compatibility, drinking capability for all personnel, compatibility with combat spectacles, and better fit and comfort.



Fig. 1. The M40 chemical-biological mask shown with hood that increases protection against liquid contamination.



Fig. 2. Overgarment issued to troops operating in forward areas (19) that do not have access to or time to use any type of decontamination procedures.

The mask alone, however, does not provide protection from substances such as nerve and blister agents that penetrate through the skin. Thus protection for the entire body should be provided. Airtight, impermeable clothing is available for personnel who must enter heavily contaminated areas. Such clothing is cumbersome and enervating because it retards release of body heat and moisture, and personnel efficiency is drastically lowered when it is worn for a long time. Although resistant to liquid chemical agents, impermeable clothing may be penetrated after a few hours exposure to heavy concentrations of agent. Consequently, liquid contamination must be neutralized or removed as soon as possible.

For field use, combat troops use the battledress overgarment (BDO) shown in Figure 2. This overgarment protects against skin contact with chemical agent vapors, aerosols, and droplets of liquid. It consists of a two-piece suit in a camouflage pattern: the jacket has a zippered front, and trousers have a fly front and zippered legs. The BDO, supplied in a vapor-barrier bag that protects it from rain, moisture, and sunlight, consists of a water-repellent outer layer of nylon–cotton and an inner layer of charcoal impregnated polyurethane foam. The overgarment is discarded once contaminated.

Collective protection enclosures are required for groups of personnel. Such enclosures must be airtight to prevent inward seepage of contamination. They can be independent units or can be formed by adequately treating the interior walls of structures, tents, airplanes, or vehicles. A supply of uncontaminated air, provided by passing ambient air through high efficiency aerosol and carbon filters, must be provided.

Simplified collection protection equipment (SCPE) (U.S. designation M20) provides such protection using lightweight elements consisting of an inflatable enclosure, a hermetically sealed filter canister, motor blower, protective entrance, and a support kit. The SCPE is designed to be used inside another structure or tent. The modular collective protection equipment (MCPE) is designed to support enclosures such as rigid wall shelters or vans. The MCPE comprises a family of items, consisting of four filter units of different sizes, external and internal protective entrances, and a motor controller. The entire system is flexible by choice of items to fit a large variety of adaptations.

Decontamination. If contaminated equipment or material does not have to be used immediately, natural aeration is an effective decontaminant procedure, as most chemical agents, including the blister and V-agents, are volatile to a certain degree. Wind accelerates their evaporation and hastens their dissipation. Rain and dew may also cause sufficient hydrolysis of some agents. Sunlight increases the surface temperatures of military equipment and thus accelerates agent evaporation.

If decontamination cannot be left to natural processes, chemical neutralizers or means of physical removal must be employed. In general, the neutralizers are of two types: chlorine-based oxidants or strong bases. Some neutralizers have been especially developed for the decontamination of chemical agents.

One such decontaminant is supertropical bleach (STB). STB is a mixture of chlorinated lime and calcium oxide containing about 30% available chlorine. It can be used either as a dry mix or as a slurry to decontaminate some equipment surfaces and terrain. The dry mix is prepared with two parts bleach to three parts earth by volume. A slurry typically consists of 40 parts STB to 60 parts by weight of water. This material is then sprayed or swabbed on the contaminated surface (see BLEACHING AGENTS). STB is an effective decontaminant for mustard, lewisite, and VX. It is less effective against nerve agents other than VX.

Decontaminating agent DS2 is a general-purpose equipment decontaminant, consisting of 70 wt % diethylenetriamine, 28 wt % ethylene glycol monomethyl ether, and 2 wt % sodium hydroxide. DS2 reacts with nerve agents and blister agents to effectively reduce their hazards within five minutes. Important limitations in the use of DS2 include: irritation to the eyes and skin, and inhalation of the vapors may be harmful; it is a combustible liquid, therefore it must not be used on hot metal surfaces such as running engines or exhaust pipes; it is not suitable for use on personal equipment such as mask or clothing or on electrical or electronic equipment; in the pure state, DS2 is noncorrosive to most metals but it may cause corrosion of aluminum, cadmium, tin, or zinc after prolonged contact; and whereas it can be used on surfaces coated with polyurethane paint, it may remove other paints, especially fairly new ones.

The M258A1 decontaminant kit, personal, is used by the individual soldier for emergency decontamination of skin and partial decontamination of personal equipment. The kit consists of three Decon 1 towelette wipes and three Decon 2 wipes, which are individually sealed in impermeable foil packets. The Decon 1 packet contains a towelette pretreated with a solution of 72 wt % ethanol, 10 wt % phenol, 5 wt % sodium hydroxide, 0.5 wt % ammonia, and the rest water. The Decon 2 packet contains a towelette impregnated with dry chloramine B and glass ampuls filled with a solution 44 wt % ethanol, 5 wt % zinc chloride, and the remainder water. The glass ampuls are contained in plastic mesh bags to prevent injury when the ampuls are broken. The M258A1 is effective against all threat agents including biological agents and toxins. It is capable of three complete decontaminations of exposed skin (hand, neck, face) and partial decontamination of personal equipment. Storage and handling of the kits require special consideration. Each of the solutions are poisonous and present a caustic burn hazard. The wipes are not to be used on eyes, wounds, or mouth. Also the kits must be stored in a dry place away from direct sunlight and flammable materials.

The M25A1 is being replaced through attrition by the M291 skin decontamination kit. This item contains six individual skin decontamination packets for the emergency decontamination of skin. Each packet contains a nonwoven fiber polybacked applicator pad impregnated with 2.8 grams of Ambergard XE-555 resin. Applicator pads have strap handles for ease of use. Individual pads are hermetically packaged in olive drab-colored, heat sealed, polyester-foil laminate material, which is notched on each corner for ease of opening. The six packets are carried in a flexible, walletlike carrying pouch constructed of nonwoven fabric. Total weight is 45 g, and it fits easily into the trousers pocket of the battledress uniform (BDU) and the protective BDO.

Besides these specially-designed decontaminants and kits there are a number of commercially available materials that will partially decontaminate chemical agents. Such materials are listed in the *U.S. Army Field Manual FM 3–5*, NBC Decontamination.

Medical Defense. The most important items of U.S. medical defense against organophosphorus nerve agents are atropine and pralidoxime chloride [51-15-0], (2-PAM), C₇H₉ClN₂O₂. These agents neutralize the effects of the anticholinesterase compounds and are capable of reactivating the inhibited enzymes. If adequate emergency treatment is immediately available, it is theoretically possible to save a high percentage of those affected by the agent. Death from nerve agent poisoning may be caused by paralysis of the respiratory muscles, airway obstruction by excessive salivary and bronchial secretions, and perhaps constriction of the bronchial tree. More recently the use of a pretreatment has been developed using pyridostigmine bromide [101-26-8], C₇H₁₃BrN₂O₂, when the threat or possibility of exposure occurs. During the 1991 Desert Storm action, over 40,000 U.S. troops were so pretreated. Similar pretreatment compounds are in use in other countries (20,21).

Immediate treatment of an exposed individual is essential. The U.S. regimen includes the pretreatment, and after exposure atropine and 2-PAM are self-administered. Further treatment includes up to two additional doses, followed by the tranquilizer Valium. As required, artificial respiration is instituted, clearing the airway if necessary. The current standard U.S. Army atropine item is the automatic injector, Atropen, designed for self-administration by the individual in the field.

Vesicant agents, such as mustard, require no special treatment once the burns have occurred. Copious washing is quite effective when used early for liquid contamination of the eyes, and soap and water removes the liquid agent from the skin. Burns resulting from mustard agent are treated like any other severe burn. The pulmonary injuries are treated symptomatically; antibiotics are used only if indicated for the control of infection.

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CHEMICALS FROM BRINE

Almost every country in the world has a source of brine containing usable minerals. Many have underground ore bodies that can be turned into brine by solution mining. The seas and oceans of the world are the largest sources of brine. Hundreds of companies extract sodium chloride, commonly called salt or halite, from the sea. Exportadora del Sal is the biggest producer, processing 6,000,000 tons of salt each year at their facility in Baja California, Mexico. Many other large and small salt producing companies can be found along the coasts of Africa, India, China, Australia, South America, and the Mediterranean and Aegean Seas. Salt is produced in the largest quantities, but compounds of magnesium, potassium, and calcium are also made from sea brine.

A second source of brine is found in terminal lakes. The Dead Sea in Israel and Jordan is an example of a large terminal lake with almost unlimited supplies of magnesium chloride, potassium chloride, and sodium chloride. More than two and a half million tons of potassium chloride are extracted from the Dead Sea each year.

Great Salt Lake, Utah, is the largest terminal lake in the United States. From its brine, salt, elemental magnesium, magnesium chloride, sodium sulfate, and potassium sulfate are produced. Other well-known terminal lakes are Qinghai Lake in China, Tuz Golu in Turkey, the Caspian Sea and Aral'skoje in the states of the former Soviet Union, and Urmia in Iran. There are thousands of small terminal lakes spread across most countries of the world. Most of these lakes contain sodium chloride, but many contain ions of magnesium, calcium, potassium, boron, lithium, sulfates, carbonates, and nitrates.

A third source of brine is found underground. Underground brines are primarily the result of ancient terminal lakes that have dried up and left brine entrained in their salt beds. These deposits may be completely underground or start at the surface. Some of these beds are hundreds of meters thick. The salt bed at the Salar de Atacama in Chile is over 300 m thick. Its bed is impregnated with brine that is being pumped to solar ponds and serves as feedstock to produce lithium chloride, potassium chloride, and magnesium chloride. Searles Lake in California is a similar ancient terminal lake. Brine from its deposit is processed to recover soda ash, borax, sodium sulfate, potassium chloride, and potassium sulfate.

A fourth source of brine is obtained through solution mining. Potash is mined in Moab, Utah by solution mining. Much of the food-grade sodium chloride in the United States, Europe, and other parts of the world is solution mined. Large beds of potassium salts in Canada and trona beds in Wyoming and California are being solution mined.

The main metals in brines throughout the world are sodium, magnesium, calcium, and potassium. Other metals, such as lithium and boron, are found in lesser amounts. The main nonmetals are chloride, sulfate, and carbonate, with nitrate occurring in a few isolated areas. A significant fraction of sodium nitrate and potassium nitrate comes from these isolated deposits. Other nonmetals produced from brine are bromine and iodine.

All of these metallic and nonmetallic ions join together in a complicated array of salts and minerals called evaporites. Several evaporites usually crystallize simultaneously in a mixture. This often makes separation into pure chemicals difficult. A list of some of the more common evaporites is given in Table 1, which also shows their chemical formulas and other mineral names.

Table 1. Common Evaporite Salts

Mineral name	CAS Registry Number	Other names	Molecular formula
anhydrite	[7778-18-9]	muriazite	CaSO ₄
antarcticite			CaCl ₂ ·6H ₂ O
aragonite	[14791-73-2]	calcite	CaCO ₃
arcanite	[14293-72-2]	sulfate of potash (SOP)	K ₂ SO ₄
bischofite	[13778-96-6]		MgCl ₂ ·6H ₂ O
bloedite	[15083-77-9]	astrakanite	Na ₂ SO ₄ ·MgSO ₄ ·4H ₂ O
borax	[1303-96-4]		Na ₂ B ₄ O ₇ ·10H ₂ O
burkeite	[12179-88-3]		Na ₂ CO ₃ ·2Na ₂ SO ₄
caliche		mixture of nitrate, chloride, and sulfate salts	
carnallite	[1318-27-0]	crackel salt	MgCl ₂ ·KCl·6H ₂ O
colemanite	[12291-65-5]		Ca ₂ B O ₁₁ ·5H ₂ O
darapskite	[12196-75-7]		NaNO ₃ ·Na ₂ SO ₄ ·H ₂ O
epsomite	[14457-55-7]	epsom salts, pickrite	MgSO ₄ ·7H ₂ O
gaylusite			Na ₂ CO ₃ ·CaCO ₃ ·5H ₂ O
glaserite	[16349-83-0]	aphthitalite	3K ₂ SO ₄ ·NaSO ₄
gypsum	[13397-24-5]	karstenite	CaSO ₄ ·2H ₂ O
halite	[14762-51-7]	salt	NaCl
hanksite	[12180-10-8]		9Na ₂ SO ₄ ·2Na ₂ CO ₃ ·KCl
hexahydrate	[17830-18-1]		MgSO ₄ ·6H ₂ O
hydrophilite			CaCl ₂
kainite	[1318-72-5]		4KCl·4MgSO ₄ ·11H ₂ O
kieserite	[14567-64-7]	wathlingenite	MgSO ₄ ·H ₂ O
kernite	[12045-87-3]		Na ₂ B ₄ O ₇ ·4H ₂ O
langbeinite	[14977-37-8]		K ₂ SO ₄ ·2MgSO ₄
leonite	[15650-69-8]		K ₂ SO ₄ ·MgSO ₄ ·4H ₂ O
loweite	[16633-52-6]		Na ₂ SO ₄ ·MgSO ₄ ·2.5H ₂ O
mirabilite	[14567-58-9]	Glauber's salt	Na ₂ SO ₄ ·10H ₂ O
nahcolite	[1575247-3]		NaHCO ₃
niter	[7757-79-1]		KNO ₃
polyhalite	[15278-29-2]	mamanite	K ₂ SO ₄ ·MgSO ₄ ·2CaSO ₄ ·2H ₂ O

pinsonite			$\text{NaCO}_3 \cdot \text{CaCO}_3 \cdot 2\text{H}_2\text{O}$
schoenite	[15491-86-8]	picromerite	$\text{K}_2\text{SO}_4 \cdot \text{MgSO}_4 \cdot 6\text{H}_2\text{O}$
sylvinite	[12174-64-0]		$\text{KCl} + \text{NaCl}$
sylvite	[14336-88-0]	muriate of potash (MOP)	KCl
syngenite		kaluszite	$\text{K}_2\text{SO}_4 \cdot \text{CaSO}_4 \cdot \text{H}_2\text{O}$
tachyhdrite	[12194-70-6]	tachyhdrite	$\text{CaCl}_2 \cdot 2\text{MgCl}_2 \cdot 12\text{H}_2\text{O}$
thenardite	[7757-82-6]	salt cake	Na_2SO_4
trona	[15243-87-5]		$\text{Na}_2\text{CO}_3 \cdot \text{NaHCO}_3 \cdot 2\text{H}_2\text{O}$
ulexite	[1319-33-1]		$\text{NaCaB}_5\text{O}_{13} \cdot 8\text{H}_2\text{O}$
vanthoffite	[15557-33-2]		$3\text{Na}_2\text{SO}_4 \cdot \text{MgSO}_4$

Recovery Processing

Solar Evaporation. Recovery of salts by solar evaporation (1–3) is favored in hot dry climates. Solar evaporation is also used in temperate zones where evaporation exceeds rainfall and in areas where seasons of hot and dry weather occur. Other factors (4,5) affecting solar pond selection are wind, humidity, cloud cover, and land terrain.

Solar salt operations can be found along the shores of the Great Salt Lake and in the San Francisco Bay area (6–10). Salt production from these areas represents 10⁰ % of the total salt produced in the United States.

Total solar salt, NaCl, produced in the world is 90 million tons. Well over that amount of salt is produced in preconcentration ponds as an intermediate step in the production of other chemicals such as potassium chloride. For example, the Dead Sea facilities produce 40 million tons of salt each year but sell none because of the high cost of transportation to markets.

Solar ponds are typically 15–50 cm deep. They are usually built over flat areas, where silts and clays have settled to make a tight soil base to prevent leakage through the bottom of the pond. In areas where soils are not tight, artificial liners of rubber or poly(vinyl chloride) (PVC) are used.

Until the 1970s, solar ponds were constructed and operated as more of an art than a science. Since then, rising land value, environmental conscientiousness, limited space, and rising costs have forced a scientific approach to solar pond optimization, design, and operation to make ponds more productive.

Where possible, solar salt is replacing vacuum salt because of rising energy costs. For example, in July the 81 × 10⁶ m² (20,000 acres) of solar ponds at Great Salt Lake Minerals Corp. evaporate over 450 million kg of water each day. This would require an equivalent of 59,000 tons of coal to supply the same energy each day. Salts formed in saturated terminal lakes or in artificial solar ponds and lakes are called evaporites (Table 1).

Seawater. Salt extraction from seawater is done by most countries having coastlines and weather conducive to evaporation. Seawater is evaporated in a series of concentration ponds until it is saturated with sodium chloride. At this point over 90⁰ % of the water has been removed, and some impurities, CaSO₄ and CaCO₃, have been crystallized. This brine, now saturated in NaCl, is transferred to crystallizer ponds where salt precipitates on the floor of the pond as more water evaporates. Brine left over from the salt crystallizers is called bitterns because of its bitter taste. Bitterns is high in MgCl₂, MgSO₄, and KCl. In some isolated cases, eg, India and China, magnesium and potassium compounds have been commercially extracted, but these represent only a small fraction of total world production.

Bays in San Francisco and San Diego are used to make salt from seawater. The combined areas are nearly 1.34 × 10⁸ m² (33,000 acres) and yield 1.3 million tons per year. Salt made from the sea is 97 to 98⁰ % pure (unwashed). The deposit is harvested in the fall after the weather turns cool and evaporation ceases (11). After harvesting, some of the salt may be washed (12,13) to obtain salt over 99⁰ % pure. Much of this salt is sold in bulk, but some is rewashed and dried in rotary kilns or fluidized-bed dryers to obtain salt of 99.8 to 99.95⁰ % purity.

The Great Salt Lake. The Great Salt Lake, located in northern Utah, is the largest lake in the western hemisphere that does not drain into an ocean. The level of the lake and the mineral concentration fluctuate depending on the weather. In 1983, annual rainfall was double normal, and runoff caused the lake to rise five feet. Again, in 1984, rain was above normal, and the lake rose another five feet, causing hundreds of millions of dollars in flood damage and diluting the mineral concentration to half its preflood value.

In 1981, seven facilities extracted minerals from Great Salt Lake brine, but flooding in 1983 and 1984 reduced the number to five. By 1992, four companies were operating. All Great Salt Lake mineral extracting facilities have solar ponds as the first stage in processing minerals from brine.

The first salt to saturate and crystallize is halite. This salt is successively followed by epsomite, schoenite, kainite, camallite, and finally bischofite. See Table 1 for the chemical composition of these minerals. In the winter, freezing temperatures cool the brine causing mirabilite, Glauber's salt, to crystallize. Solar pond end brine, called bitterns, contains 35⁰ % magnesium chloride. These bitterns are used as a feedstock to make magnesium metal, bischofite flake, dust suppressants, freeze prevention and fertilizer sprays, and they are used in ion-exchange resins. Figure 1 depicts a multiproduct facility that uses Great Salt Lake Brine.

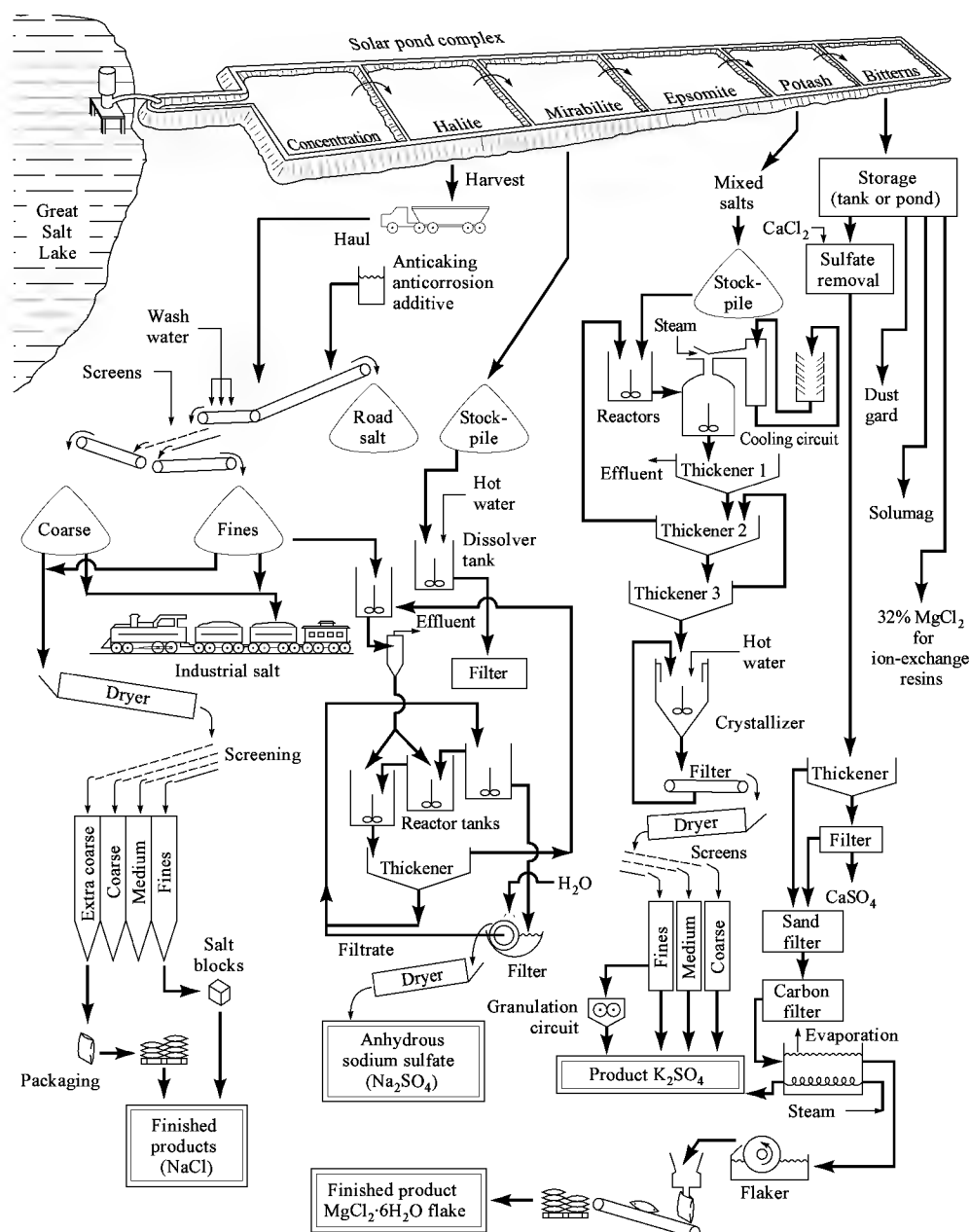


Fig. 1. Abbreviated flow sheet of the multiproducts of Great Salt Lake Minerals Corporation.

Solution Mining. Solution mining, also known as brining, is the recovery of sodium chloride or any soluble salt in an underground deposit by dissolving it *in situ* and forcing the resultant solution to the surface.

Solution mining produced nearly 23 million metric tons of salt in 1989 representing more than half of the total U.S. salt production (14). Salt brine is made from bedded salt at more than 18 different locations and from 17 salt domes (15). Bedded salt of the salina formation is the most widely and intensively exploited by solution mining. Enormous reserves of salina salt are available. Cost of solution mining salt is usually less than the cost of salt produced by dry mining. The method is particularly good where salt deposits are deep and dry mining would not be feasible.

The essentials of solution mining a salt dome are shown in Figure 2. Production rate of any given mine is limited to the dissolving rate of the salt to bring it close to saturation. The flow rates of the injected water controls the rate of outflowing brine. Adjustment of this injected brine therefore controls the degree of saturation of recovered brine. Since energy must be used to remove all the water to recover sodium chloride, it is important to keep brine near saturation. Frequently, in thin-bed salt strata, two wells (16) are used. The wells communicate through hydraulically formed fracture channels.

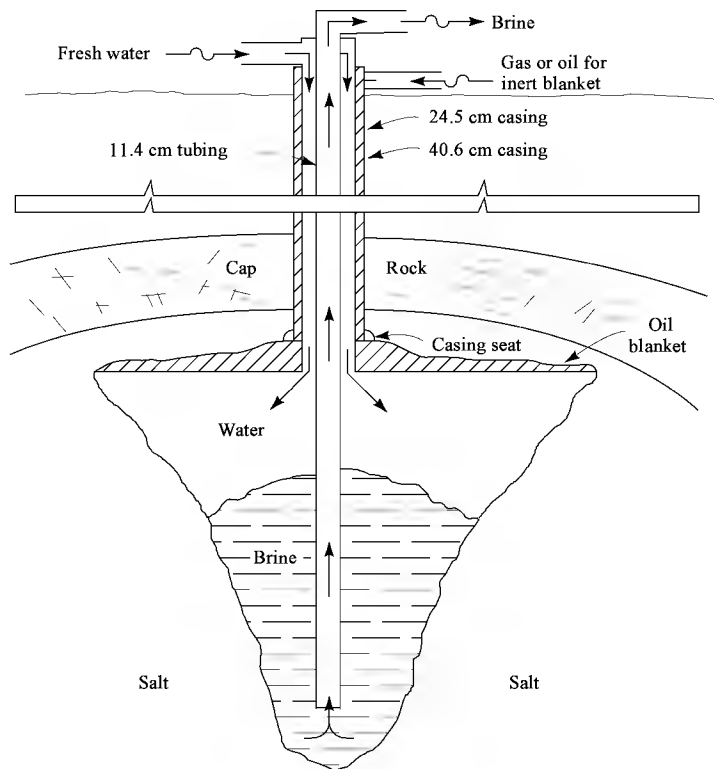


Fig. 2. Typical solution mining operation in a salt dome (9).

An environmental risk in solution mining is surface subsidence. This risk is greatest with embedded salt. No cases of salt subsidence have been reported in mining domes that have been mined according to standard industry approved practice in the United States, but some have been seen in other countries. One side benefit of dome solution mining is use of the cavities later for storage of industrial fluids, chiefly petroleum and natural gas. Solution mining for sodium chloride is extensively used in Europe and the states of the former Soviet Union.

Minerals from Brine

BORON COMPOUNDS

Occurrence. Brine found in Searles Lake, California is the only brine source where boron is produced commercially. Other brine bodies such as the Great Salt Lake or brine from thermal wells at the Salton Sea have been considered but have not been exploited. Brines at the Salar de Atacama in Chile also contain boron, but it is not presently extracted. Boron is found in two underground ores, ulexite and colemanite. Research and pilot-plant studies have been completed to solution mine these ores, but as yet it is not done commercially. Boron is found in many different evaporite deposits (17).

Recovery Process. Boron values are recovered from brine of Searles Lake by North American Chemicals Corp. In one process the brine is heated to remove some water and burkeite. The remaining brine is cooled to remove potassium chloride. This cooled brine is then transferred to another crystallizer where borax pentahydrate, $\text{Na}_2\text{B}_4\text{O}_7 \cdot 5\text{H}_2\text{O}$, precipitates (18). In a separate process, boron is removed by liquid-liquid extraction followed by stripping with dilute sulfuric acid (19). Evaporator-crystallizers are used to recover boric acid [10043-35-3], H_3BO_3 . In a third process, borax is recovered by refrigerating a carbonated brine.

Economic Aspects and Uses. The principal producers in the United States are U.S. Borax and Chemical Corp., North American Chemicals Co., and American Borate Corp. Their combined annual capacity in 1989 was reported to be 735,000 metric tons of equivalent boron oxide [1303-86-2], B_2O_3 (20). Of this tonnage, 50% is exported. About 30% of boron compounds are used in glass fiber insulation. Another 30% is used in other type fibers and borosilicate glasses. Boron is also used in soaps and detergents, fire retardants, and agriculture (see BORON COMPOUNDS).

BROMINE

Occurrence. Bromine [7726-95-6] is found in seawater and in underground brine deposits of marine origin (21). Bromine (qv) is also found in Dead Sea brine and is currently being produced there by the Dead Sea Works. The earliest commercial production of bromine in the United States, in the mid-1800s, made use of a brine well in Freeport, Pennsylvania (22). Later, recovery of bromine from brine wells in Midland County, Michigan was developed. Brines in Michigan, Ohio, and West Virginia supplied the principal portion of production in the United States until 1935. Michigan brines are still a source of bromine today. A significant source of bromine in 1991 came from wells in southwest Arkansas. Bromine is found in Searles Lake brine and was produced there at one time, but commercial extraction has been discontinued.

Recovery Process. Commercial processes depend on the oxidation of bromide to bromine. Most of the liberated bromine remains dissolved in the brine. The brine is then stripped of bromine followed by recovery of bromine from the stripping agent. Subsequent purification by distillation is often a final step. Direct electrolysis was used at one time for the oxidation step. Manganese dioxide has also been used as an oxidant. Most present day processes use chlorine:



Steam stripping or steaming-out (Fig. 3), is the only method currently used in the United States to remove elemental bromine from the brine. This method is economical for brines containing bromine above 1000 ppm.

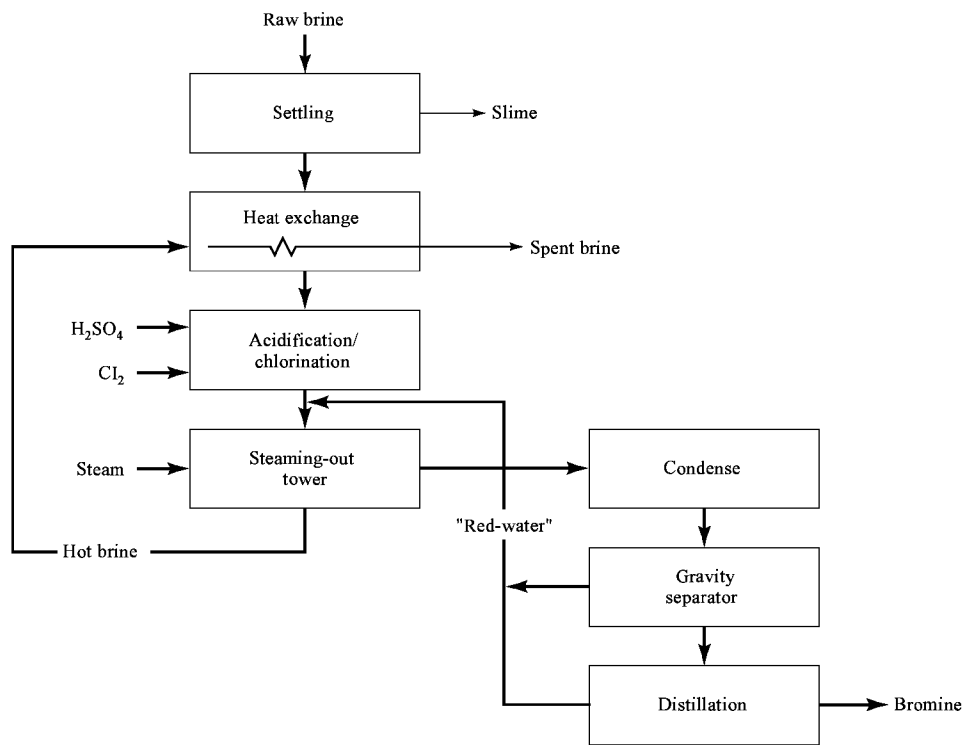


Fig. 3. Steaming-out process for recovery of bromine from high bromide brines (22).

Older methods of stripping used with concentrations below 1000 ppm utilize a stream of air flowing countercurrent to the brine stream. The bromine is then recovered from the air with wet scrap iron, ammonia, sodium carbonate, or sulfur dioxide (23–25).

Economic Aspects and Uses. The United States produced 174,600 tons of bromine in 1989 (26). Over 95% of this was produced in southeastern Arkansas. The remainder was produced from Michigan brines. Production of bromine from Seales Lake brine has been discontinued.

About 10% is marketed in elemental form. Eighteen percent is converted to ethylene dibromide [106-93-4] for use in gasoline and 30% is used in fire retardants. Fifteen percent is used as a soil fumigant methyl bromide [74-83-9]. Other commercial forms are alkali metal bromides, ammonium bromide [12124-97-9], and hydrobromic acid [10035-10-6].

CALCIUM CHLORIDE

Occurrence. Brines are the main commercial source of calcium chloride [10043-52-4]. Some brines of Michigan, Ohio, West Virginia, Utah, and California contain over 4% calcium (27). Michigan is the leading state in natural calcium chloride production with California a distant second.

A former commercially important source of calcium chloride was as a by-product of the Solvay process used to produce soda ash (28). Because of environmental concerns and high energy costs, the Solvay process has been discontinued in the United States though it is still used extensively elsewhere in the world (see CALCIUM COMPOUNDS).

Recovery Process. Because of its high solubility compared to that of other brine constituents, calcium chloride is the final constituent recovered in a multiproduct brine processing operation. Magnesium chloride is another highly soluble component that may occur with the calcium chloride. Separation of magnesium ions may be accomplished by precipitating magnesium hydroxide or by crystallizing tachyhydrite, $CaCl_2 \cdot 2MgCl_2 \cdot 12H_2O$ (29,30) or $2CaCl_2 \cdot MgCl_2 \cdot 2H_2O$. Both yield additional calcium chloride liquor. Calcium chloride flake can be made similar to magnesium flake (Fig. 4).

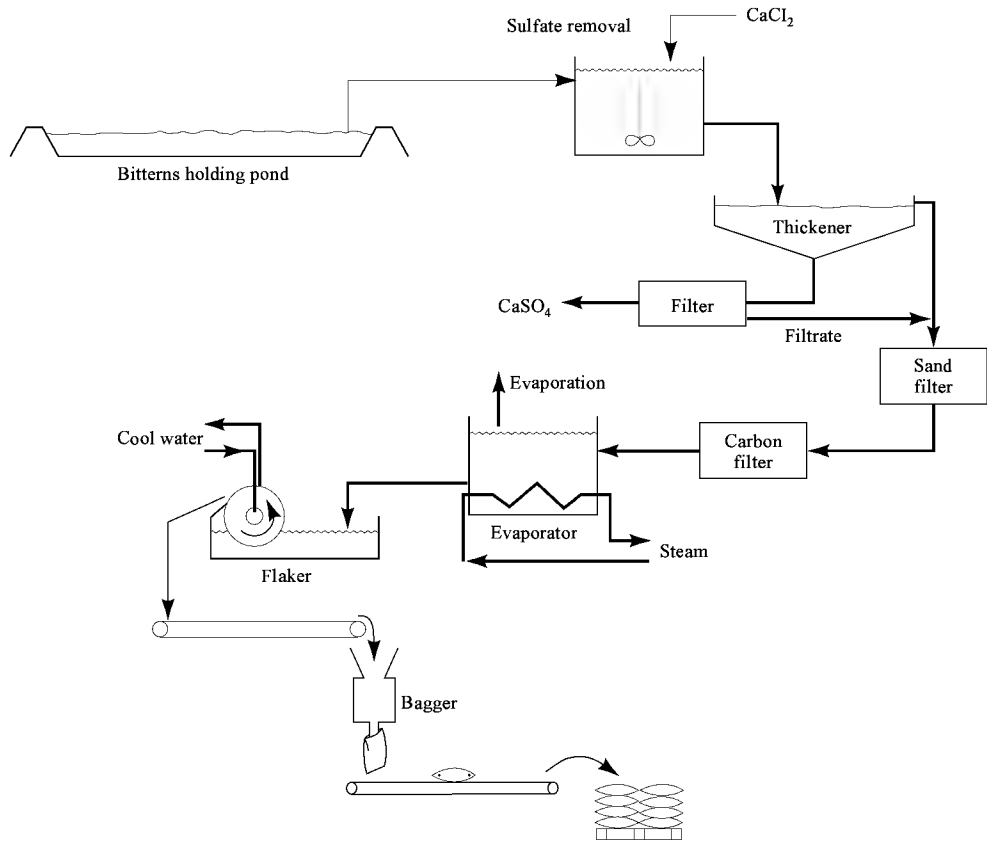


Fig. 4. Magnesium chloride flaking circuit $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$.

Economic Aspects and Uses. Total production of calcium chloride in 1989 was 873,000 tons (31). Most of this was produced from Michigan brines. The principal use of calcium chloride is to melt snow and ice from roads. It is also used in dust control, concrete setting control, and various industrial uses.

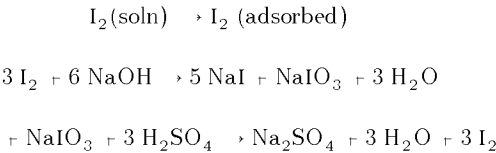
IODINE

Occurrence. Iodine [7553-56-2] is widely distributed in the lithosphere at low concentrations (about 0.3 ppm) (32). It is present in seawater at a concentration of 0.05 ppm (33). Certain marine plants concentrate iodine to higher levels than occur in the sea brine; these plants have been used for their iodine content. A significant source of iodine is caliche deposits of the Atacama Desert, Chile. About 40% of the free world's iodine was produced in Japan from natural gas wells (34), but production from Atacama Desert caliche deposits is relatively inexpensive and on the increase. By 1992, Chile was the primary world producer. In the United States, underground brine is the sole commercial source of iodine (35). Such brine can be found in the northern Oklahoma oil fields originating in the Mississippian geological system (see IODINE AND IODINE COMPOUNDS).

Recovery Process. In past years iodine was recovered at Long Beach, California from oil field brine and from natural brines near Shreveport, Louisiana (36,37). The silver process was used. Silver nitrate reacts with sodium iodide to precipitate silver iodide. Added iron forms ferrous iodide and free silver. The ferrous iodide then reacts with chlorine gas to release free iodine. After 1966, the silver process was replaced with the blowing-out process similar to the bromine process.

Later, more concentrated brines of the Midland, Michigan producers displaced the California producers. In 1976, Houston Chemicals began recovery using the blowing-out process from underground brines of the Anadarko Basin in northwestern Oklahoma. Annual capacity was 900 metric tons (38). In 1991, nearly all of the iodine produced was made from Oklahoma brines by a blowing-out process.

Japan was the leading producer of iodine in the 1980s, producing nearly 7000 metric tons per year. Elemental iodine was released into brine by treatment with sodium nitrate or chlorine. The free iodine was then adsorbed on activated carbon. It was stripped from the carbon with sodium hydroxide followed by acidification to form a slurry of elemental iodine:



A large reserve of caliche ore bearing iodine is being processed in the Atacama Desert. Production of iodine there is relatively inexpensive. About 40% of the world supply of iodine is made from these Chilean deposits. The process consists of leaching the caliche with water. Brine is stripped of iodine using an organic solvent. The iodine is then removed from the solvent to form a slurry. Solid-phase iodine is separated from the slurry in conventional flotation cells, dried, and packaged. Details of the process are proprietary.

Economic Aspects and Uses. Most of the iodine used in the United States comes from Japan and Chile. The United States produces 10% of the world supply but consumes 30%. Production in Chile appears to be relatively low cost, and the product there presently controls prices. Iodine is produced in Woodward and Vici, Oklahoma. These two locations produce about 30% of the 4000 tons used yearly in the United States. Total world consumption is 10,000 to 12,000 tons per year. Prices range from \$20.00/kg in 1988 to \$12.5/kg in 1991.

A primary use for iodine is as a catalyst in the production of acetic acid (qv) (39). Iodine is converted to compounds used in rubber, stabilizers, animal feed supplements, colorants, pharmaceuticals, sanitary products, and photographic products.

LITHIUM

Occurrence. Numerous brines contain lithium in minor concentrations. Commercially valuable natural brines are located at Silver Peak, Nevada (400 ppm) (40,41), and at Seardes Lake, California (50 ppm) (42,43). Great Salt Lake brine contains 40 ppm and is a source not yet exploited. Seawater contains less than 0.2 ppm. Lithium production started at Silver Peak in the 1970s. The concentration of lithium in the brine is diminishing, and now the principal production occurs from brine in the Salar de Atacama, Chile.

Lithium brines with commercial potential are found in the Altiplano of Bolivia and Argentina, in salt beds of Chile, and in several salt beds in central and western China.

Recovery Process. Lithium is extracted from brine at Silver Peak Marsh, Nevada, and at the Salar de Atacama, Chile. Both processes were developed by Foote Mineral Corp. The process at Silver Peak consists of pumping shallow underground wells to solar ponds where brines are concentrated to over 5000 ppm. Lithium ion is then removed by precipitation with soda ash to form a high purity lithium carbonate [554-13-2]. At the Atacama, virgin brine with nearly 3000 ppm lithium is concentrated to near saturation in lithium chloride [7447-41-8]. This brine is then shipped to Antofagasta, Chile where it is combined with soda ash to form lithium carbonate.

Lithium extracted from Seardes Lake brine has been discontinued (42).

Economic Aspects and Uses. In 1976, one-third of the lithium produced in the United States was extracted from brines of Seardes Lake and Silver Peak (44,45). Since then, lithium production at Seardes Lake has been discontinued and the lithium concentration at Silver Peak is decreasing. During the 1980s lithium extraction was started at the Salar de Atacama, Chile. This is the largest lithium production plant in the world using brine as its raw material.

The United States produces and consumes about one-half of all the world production. Ore grades for the two principal nonbrine producers are becoming poor, and imports of brine-based lithium carbonate are increasing.

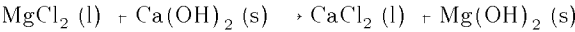
About 65% of the lithium is used as a cell-bath additive in aluminum production and in ceramics and glass. Lithium batteries enjoy increasing popularity leading to steady growth in this market. Other uses are in lubricants and synthetic rubber (46). Since lithium is a light, strong metal, it finds applications in aerospace metals and alloys where a light metal is needed (see LITHIUM AND LITHIUM COMPOUNDS).

MAGNESIUM COMPOUNDS

Occurrence. Magnesium hydroxide [1309-42-8] and magnesium chloride [7786-30-3] are two commercially important magnesium compounds recovered directly from natural brines. From these compounds many other compounds of magnesium are made such as elemental magnesium [7439-95-4] and magnesia [1309-48-4]. Other important compounds containing magnesium are epsomite, schoenite, kainite, and carnallite. The principal magnesium sources are seawater (1300 ppm), Great Salt Lake (1.1% Mg) (47), underground brines near the surface east of Wendover, Utah (1%) (48), subterranean brines in Michigan (0.7–2.5%) (49–51), and brine from the Yates formation in the Midland Basin of west Texas (3%) (52). Other subterranean brines containing magnesium at high concentration are known (53) but are not commercially extracted.

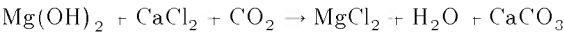
Besides the oceans, there are vast reserves of magnesium chloride in the Dead Sea; Qaidam Basin, China; and many salars of South America.

Recovery Process. Magnesium hydroxide can be recovered in relatively pure form either from brine or from an intermediate plant liquor by increasing alkalinity, for example:



Better recoveries can be made by replacing calcium hydroxide [1305-62-0] with dolomite [39445-23-3] that has been calcined. Sometimes NaOH is used when low calcium in the product is required.

Recovery of magnesium chloride as a direct product is usually economically feasible only as a by-product. Like calcium chloride, magnesium chloride is highly soluble and is extracted at the end of a series of processes that first removes the less soluble products as the magnesium ion concentrates. In Michigan brines, NaCl, Br₂, I₂, CaCl₂, Mg(OH)₂, and KCl are coproducts. At Great Salt Lake, NaCl, Na₂SO₄, and K₂SO₄ are coproducts, and MgCl₂ is the last to be recovered. In a current process for Michigan Basin brines, pure MgCl₂ liquor is formed by reaction of previously precipitated Mg(OH)₂ with stack gas and concentrated brine:



End brines at Wendover, Utah and the Great Salt Lake have concentrations up to 36% MgCl₂. At Great Salt Lake Minerals Corp. this highly concentrated brine is artificially evaporated to remove 15% of the water. The hot solution is then cooled to form bischofite, MgCl₂·6H₂O. Figure 4 shows the process.

Magnesium metal is produced by the electrolysis of molten MgCl₂ by two different processes. In The Dow Chemical Company seawater process, MgCl₂ liquor is formed by reaction of lime [1305-78-8], CaO, or dolomite with seawater to form Mg(OH)₂ and then neutralized with HCl to form MgCl₂. The slurry is dried to a hydrous cell feed containing about 70% MgCl₂. The other process used by MagCorp with Great Salt Lake brines recovers anhydrous MgCl₂ directly from concentrated brine by spray drying. In both cases, elemental magnesium and chlorine gas are formed in the cells (see MAGNESIUM AND MAGNESIUM ALLOYS).

The Dead Sea has an unlimited reserve of MgCl₂. Presently the Arab Potash Co. discharges its MgCl₂ brine back to the sea, but its neighbor to the west, The Dead Sea Works, produces MgO from some of their concentrated brines.

Magnesium oxide [1309-48-4] has also been produced from concentrated ocean brines that have first been used to make sodium chloride in solar ponds. The process is basically to form Mg(OH)₂ by adding dolomite or lime to the brine and then to burn Mg(OH)₂ to MgO.

Economic Aspects and Uses. Magnesium hydroxide and magnesium chloride are used as a basic feedstock to make elemental magnesium, MgO refractories, and reactive chemicals. One hundred and sixty thousand tons of magnesium metal were produced in the United States in 1989 in addition to 1,013,000 tons of MgO equivalent in magnesium compounds (qv) (54).

Magnesium is removed from brines of the Great Salt Lake in the form of magnesium chloride. This is then used to make elemental magnesium, dust suppressants, and bischofite flake. Magnesium chloride is also used in drilling mud, ion-exchange resins, oxi-chloral cements, fertilizers, and miscellaneous industrial uses.

POTASSIUM COMPOUNDS

Occurrence. Muriate of potash [7447-40-7], KCl, and sulfate of potash [7778-80-5], K₂SO₄, are produced from brines in the United States (48,55–59). Three brine potash operations are located in Utah at Moab, Ogden, and Wendover and one in California at Searles Lake. Operations in Searles Lake produce both muriate and sulfate of potash. The Ogden operation produces sulfate of potash. The others produce muriate.

Recovery Process. The Texas Gulf, Cane Creek potash operation (60) of Moab, Utah produces KCl by solution mining (61–64). Brine is pumped from underground to 1.6 × 10⁶ m² (400 acres) of solar ponds where a mixture of KCl and NaCl is crystallized in a salt mass called sylvinite. Sylvinite is removed from the ponds with scraper-loaders and hauled to a central pit. The salts are then transported to the refinery in a slurry line. KCl is separated from the NaCl by flotation. The flotation process is standard throughout the industry and is the same process used to separate KCl from impurities in a carnallite decomposition process explained later. An amine collector is used as one of the reagents.

Production of KCl at the Wendover, Utah operation employs a large 7000 acre complex of solar ponds. Both shallow brine wells and deeper wells are used to pump brine into the pond complex. In the preconcentration ponds water is evaporated and sodium chloride is crystallized. Later the brine is transferred to production ponds where sylvinite is deposited. Brine is then transferred to other ponds where carnallite is crystallized. Sylvinite is removed from drained ponds with self-loading scrapers and taken to the plant where KCl is separated by flotation with an amine oil collector. The carnallite, KCl·MgCl₂·6H₂O, is decomposed by leaching with water. The water dissolves MgCl₂ and leaves KCl and impurities, mainly NaCl. KCl is then separated from impurities by conventional flotation.

Great Salt Lake Minerals Corp. near Ogden, Utah, produces potassium sulfate and several other products from Great Salt Lake brines. Presently 81 × 10⁶ m² (20,000 acres) is divided into 80 solar ponds with 81 million m² of expansion scheduled in 1992. Two years are required to process brine through the ponds. During the two years, salts crystallize in the following sequence: NaCl, MgSO₄·7H₂O, MgSO₄·K₂SO₄·6H₂O, MgSO₄·KCl·2.75H₂O, MgCl₂·KCl·6H₂O, and MgCl₂·6H₂O. In the winter Na₂SO₄·10H₂O crystallizes. All the salts containing potassium are harvested from the ponds and hauled into the refinery where impurities are leached out and remaining potassium is converted to K₂SO₄. In addition to potassium, three other primary products are made as shown in the flow of Figure 1.

Economic Aspects and Uses. Total world production of potassium products is 29,000,000 tons per year (65). Potassium chloride is removed from brine at Moab, and Wendover, Utah, and at Searles Lake, California. Potassium sulfate is made from Great Salt Lake brine by Great Salt Lake Minerals Corp., which is the largest producer of solar potassium sulfate in the world. Combined, these U.S. facilities still produce a relatively small percentage of potash fertilizers in the world. Production from the Dead Sea, for example, is 10 times greater than production of potassium from brines in the United States. More than 95% of all the potassium produced is used in fertilizer blends. The remainder is converted to other potassium chemicals for industrial use (see POTASSIUM COMPOUNDS).

Domestic potash production supplies one-third of U.S. consumption. The rest comes from mines in Canada and Europe. Prices of both KCl and K₂SO₄ fluctuate. KCl ranges between 65 to 95 dollars per ton. Sulfate of potash sells for 150 to 190 dollars per ton.

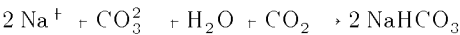
SODIUM CARBONATE

Occurrence. The brines of Searles Lake, California are the sole brine source of sodium carbonate [497-19-8] (soda ash) production in the United States. There is a large underground deposit of sodium carbonate brine in the Sua Pan area of Botswana, Africa (66). Another potential source is Owens Lake, California. Owens Lake brines were used to produce soda ash but were discontinued in 1967.

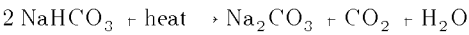
In the mid-1980s FMC began solution mining trona beds at Green River, Wyoming to produce soda ash. NaTech is currently developing a solution mining process for sodium bicarbonate [144-55-8] in Colorado.

Recovery Process. Presently North American Chemical Co. at Searles Lake is the only significant producer in the world of sodium carbonate from brine (1,000,000 t yr).

Another operation using the same process as North American Chemical Co. is scheduled to produce 300,000 tons per year at Sua Pan, Botswana; however, by 1992 the plant had been completed, but full-scale production had not been achieved. The process is based on converting all sodium carbonate in the brine to sodium bicarbonate by adding CO₂:



Impurities remain in the brine solution and the sodium bicarbonate crystallizes and is filtered from the liquor. The bicarbonate is then converted to carbonate by heating:



Carbon dioxide (qv) is recycled back again to the carbonation vessels.

In 1976, over 3,000,000 tons of soda ash were produced in the United States using the Solvay process. This process has been discontinued in the United States because of pollution problems and high processing costs. It is still an important process in other countries.

Economic Aspects and Uses. North American Chemical Co. at Seardes Lake is now the only producer of soda ash from naturally occurring brine in the United States. Production from brine represents only about 10^o % of U.S. production (67).

Half of all sodium carbonate is used in glass production. One-fourth is used to make other chemicals and the remainder is used in detergents and paper production (see [ALKALI AND CHLORINE PRODUCTS](#), [SODIUM CARBONATE](#)).

SODIUM CHLORIDE

Occurrence. About half of all the sodium chloride [7647-14-5] produced in the world is from brine. Approximately one hundred million tons per year are produced from brines of the ocean, terminal lakes, subterranean aquifers, and solution mining (14). Sodium is found in large quantities in most areas of the world. Its quantity is so large that prices in some locations are only a few dollars per ton. Many areas have millions of tons but prices are so low that it is not economical to mine or process the salt. The largest exposed sodium chloride bed is at the Salar de Uyuni, Bolivia, but Bolivia is landlocked and very little of the salt can be processed and sold at a profit.

Recovery Process. Figure 5 shows a typical scheme for processing sodium chloride. There are two main processes. One is to flood solar ponds with brine and evaporate the water leaving sodium chloride crystallized on the pond floor. The other is to artificially evaporate the brine in evaporative crystallizers. Industrial salt is made from solar ponds, whereas food-grade salt, prepared for human consumption, is mostly produced in the crystallizers.

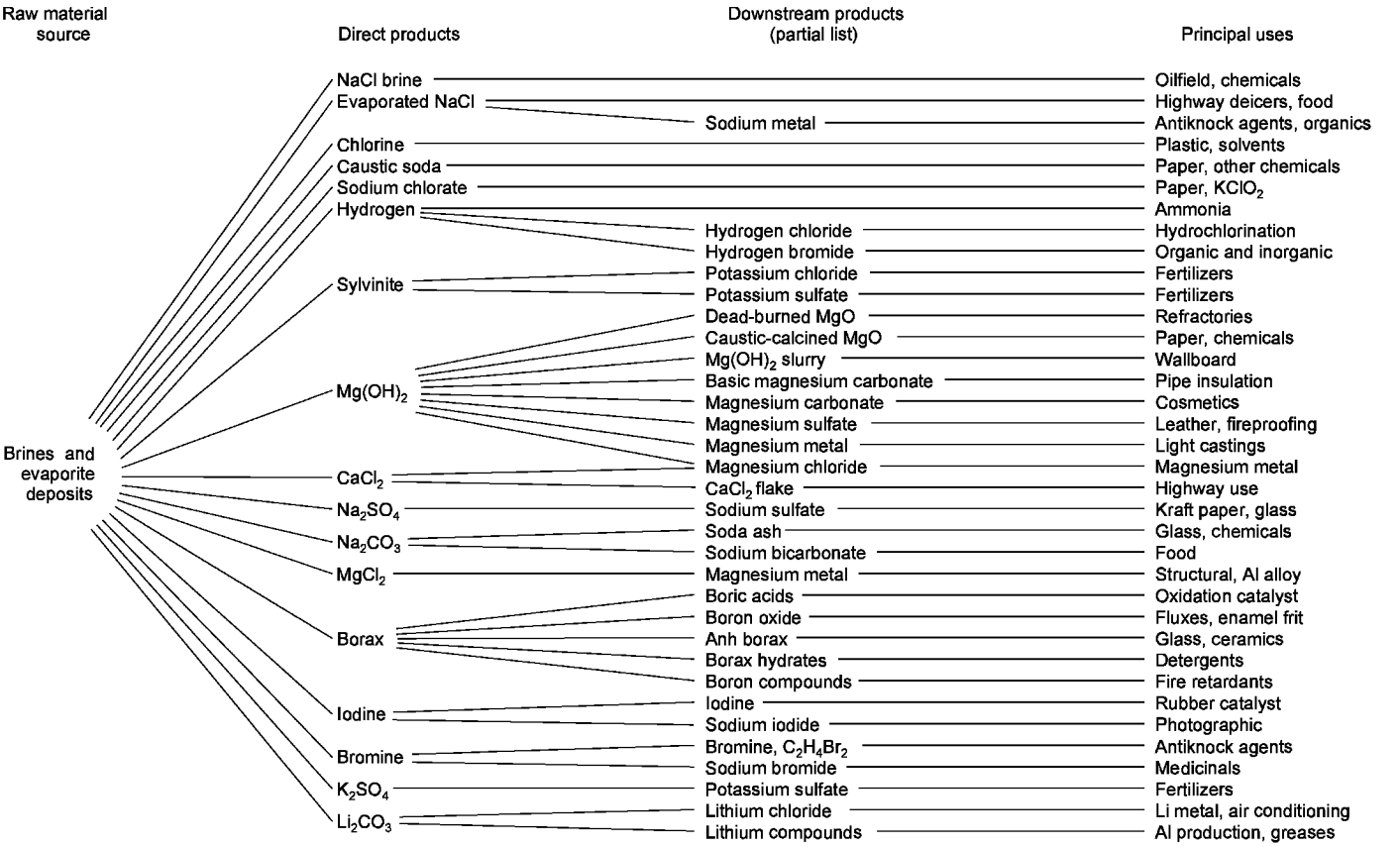


Fig. 5. The brine chemical industry and some of its products.

Economic Aspects and Uses. The United States is the largest producer of salt in the world. In 1988, 20^o % of the world's salt (14) was made in the United States. Salt continues to be one of the most heavily traded chemical ores in the world representing nearly 65^o % of all seaborne mineral trade. World consumption is over 200 million tons per year. Most of this salt is made from brines. Salt is used directly or indirectly in 14,000 different products (68).

Salt has had a significant impact on the economies of some countries, and in some places it still does. Salt was the first chemical recognized and used in ancient times (69). It was first used in food for taste enhancement and as a preservative (see [SODIUM COMPOUNDS](#)).

Today most salt is used to make caustic soda and chlorine (see [ALKALI AND CHLORINE PRODUCTS](#), [CHLORINE AND SODIUM HYDROXIDE](#)). These chemicals are used in thousands of household products. The next biggest use is for highway deicing. Other uses are for water softening, livestock feeds, meat packing, and foodstuffs.

SODIUM SULFATE

Occurrence. In the United States natural sodium sulfate brines are found at Seardes Lake, at the shallow castile formation underlying Terry and Gains counties in Texas, and at the Great Salt Lake.

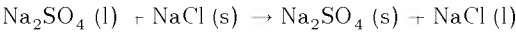
Other natural sodium sulfate brines of commercial importance are found in dry lake beds of southwestern Saskatchewan, Canada (70); Laguna del Ray in Coahuila, Mexico; the Gulf of Kara-bogaz of the former USSR; and western China.

Recovery Process. The process for making sodium sulfate [7757-82-6] is different at each facility extracting it from brine. One step common to all facilities is a cooling step to form Glauber's salt followed by a purification and recrystallization step to form anhydrous sodium sulfate.

In Texas, brine is pumped from underground deposits. Sodium chloride is added to bring the brine near saturation. This solution is then chilled to 8°C to crystallize Glauber's salt (71). Anhydrous Na₂SO₄ is recovered by artificially evaporating the liquor formed by remelting the Glauber's salt.

At Seardes Lake, sodium sulfate is recovered as one of three coproducts in a series of complex operations where soda ash and borax are also recovered from the brine. Anhydrous sodium sulfate is recovered by artificially evaporating the water from Glauber's salt.

In processing Great Salt Lake brine, Glauber's salt is crystallized in solar ponds by cooling during the winter. This salt is harvested and stockpiled when it is still cold. Once the stockpile has drained, the Glauber's salt is stable in the solid phase throughout the year and can be reclaimed at any time. Reclaimed Glauber's salt is redissolved in hot water at the refining plant. The resulting liquor is filtered to remove insolubles and then reacts with sodium chloride to form anhydrous sodium sulfate according to the reaction:



Economic Aspects and Uses. About 50° of all sodium sulfate produced in the United States is from brine. In 1988, 410,000 tons were produced from brine. Most of the production is from North American Chemicals Co. Ozark-Mahoning at Brownfield and Seagraves, Texas produce 25° and Great Salt Lake Minerals and Chemicals Corp. produce 5°.

Of the sodium sulfate produced in the United States the paper industry consumes 36°, 45° is used in detergents, and 10° in the glass industry (72). Powdered detergents are on the decline in favor of liquids that do not use sodium sulfate. Since the pulp and paper industry are also using less, the price of sodium sulfate is fluctuating (see SODIUM COMPOUNDS).

Economic Aspects and Uses

Demand and prices for chemicals from brine has fluctuated in the last 10 years. Table 2 shows a price list (73) of some of the main chemicals extracted from brines in 1991.

Table 2. 1991 Prices for Chemicals Extracted from Brine

Chemical	Price	
	\$ kg	\$ t
boron compounds		
borax, tech., anhyd., bagged, 99°		760
borax decahydrate, bagged		285
boric acid, bagged, 99.9°		775
bromine		
drums	2.27	
bulk in tank cars	0.95	
calcium chloride		
flaked, anhyd., bagged, 94–97°		358
bulk, anhyd., 80°		182
iodine		
USP in drums	37.40	
crude in drums	13.00	
lithium compounds		
lithium carbonate, bagged	4.03	
lithium sulfate, anhyd., bagged	7.72	
magnesium compounds		
magnesia, bulk, tech.		364
magnesia, dead burned, bulk		432
magnesium chloride, hydrous, bagged, 99°	0.32	
magnesium metal 99.8°	3.15	
potassium compounds		
potassium chloride, bulk		87
potassium nitrate, bulk		353
potassium sulfate, bulk		193
sodium carbonate		
decahydrates, bagged		291
soda ash, bagged, light		161
soda ash, bulk		108
sodium chloride		
bulk		66
bagged		111
sodium sulfate		68

Figure 5 illustrates some principal brine evaporites and their derivative products. Some of these chemicals find application in thousands of household items. Sodium chloride alone has over 14,000 different uses (68).

New technology and development of brine reserves are increasing each year in the United States and abroad. This affects the uses and price of brine chemicals. For example, development of the Salar de Atacama in Chile in the 1980s as the largest producer of brine lithium in the world has affected lithium production and prices worldwide. Lithium production from Seardes Lake brine has been discontinued, and the Silver Peak operation in Nevada is in a slow production decline caused by weaker brine grades.

There has been much interest in making chemicals from brine because of the low expense compared to alternative methods. Lithium, for example, had been mostly produced from spodumene ore, but now most is produced from brine. Those now producing from ore are seriously researching brine reserves and contemplating converting to brine sources before the turn of the century. Similarly, solar salt has cost advantages over mined rock salt. Potassium chloride produced from brine has more than doubled from 1980 to 1990.

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CHEMOMETRICS

Chemometrics has been defined as the chemical discipline that uses mathematical and statistical methods to design or select optimal measurement procedures and experiments, and to provide maximum chemical information by analyzing chemical data. As a subdiscipline of chemistry, the field emerged in the late 1960s and early 1970s as an outgrowth of pattern recognition and other techniques of artificial intelligence and applied mathematics.

Artificial intelligence is the field that is concerned with using computers to mimic or model human intelligence. Machines lack the ability of living systems to learn and adapt. In artificial intelligence, research is conducted on how computers can provide adaptive solutions to changing problems. A common example is programming a computer to play chess (1). Other examples of artificial intelligence can be found in the literature (2–4).

Pattern recognition methods were originally used to address data processing problems in applications such as alphanumeric character recognition, speech analysis, fingerprint identification, and scene analysis. The term pattern recognition refers to a variety of computer tools that can be used to predict a property of an object where the property is not itself measured, but rather is inferred from a set of experimental measurements made on the object that are indirectly related to the property. An example is computer recognition of handwritten alphanumeric characters. In a pattern recognition approach, a set of measurements would be made on many samples of handwriting for which the correct corresponding true letters and or numbers are known and fed into the computer. The measurements might be obtained by optically scanning the field of each handwritten letter, digitally recording the intensity of reflected light in a systematic way over, eg, 100 points in each field. The computer is instructed to develop a classification rule for deciphering all 26 handwritten letters of the alphabet and the 10 numerical characters based on these handwriting samples with their given printed equivalents. A new sample of handwriting, hitherto unseen by the computer, can then be deciphered by feeding in the optical scan and asking the computer to apply the classification rule to the new data.

Using a pattern recognition approach means: given a collection of objects characterized by a set of measurements made on each object, the goal is to find or predict a property of the objects that is not directly measurable or measured but that is thought to be indirectly related to the measurements via some unknown or undetermined relationship. In the context of chemistry, a collection of objects is a set of chemical samples or measurements. Probably the first application of pattern recognition to chemical data was done in 1966 where a classification rule was developed to distinguish paraffins from olefins on the basis of mass spectral measurements (1). In 1969 mass spectral data were used to determine the molecular formula of molecules containing carbon, hydrogen, oxygen, and nitrogen (5). Functional group and molecular structural information have been extracted by pattern recognition methods from infrared spectra (6), mass spectra (7), and nuclear magnetic resonance (nmr) spectra (8).

In 1972, the concept of pattern recognition as a general problem solving tool for a broad scope of chemical applications was introduced (9,10). Much of the experimental work in chemistry deals with predicting or inferring properties of objects from measurements that are only indirectly related to the properties. For example, spectroscopic methods do not provide a measure of molecular structure directly, but, rather, indirectly as a result of the effect of the relative location of atoms on the electronic environment in the molecule. That is, structural information is inferred from frequency shifts, band intensities, and fine structure. Many other types of properties are also studied by this indirect observation, eg, reactivity, elasticity, and permeability, for which *a priori* theoretical models are unknown, imperfect, or too complicated for practical use. Also, it is often desirable to predict a property even though that property is actually measurable. Examples are predicting the performance of a mechanical part by means of nondestructive testing (qv) methods and predicting the biological activity of a pharmaceutical before it is synthesized.

A variable is a facet or aspect of a sample that can be measured, such as a chloride ion concentration, density, boiling point, absorption spectrum, or chromatographic peak. A measurement is the experimentally determined value used to characterize a sample. If a sample variable is iron concentration, then a measurement is the experimentally determined numerical value of iron concentration. Spectral methods such as ir, nmr, uv vis, and various x-ray techniques yield wavelength or frequency measurements of characteristic absorption peaks or digitized absorption spectra at regular wavelength intervals; mass spectral data give abundances of ion fragments; and atomic absorption measurements correlate to elemental concentrations (see ANALYTICAL METHODS; AUTOMATED INSTRUMENTATION). Separation techniques supply measurements of retention time in the case of chromatography (qv), or position, in the case of electrophoresis (qv), as well as quantity of material. Chemometrics can be employed to examine spectral or thermodynamic data of chemical compounds, the composition of mixtures, or mechanisms of reactions (11).

The ordered set of measurements made on each sample is called a data vector. The group of data vectors, identically ordered, for all of the samples is called the data matrix. If the data matrix is arranged such that successive rows of the matrix correspond to the different samples, then the columns correspond to the variables as in Figure 1. Each variable, or aspect of the sample that is measured, defines an axis in space; the samples thus possess a data structure when plotted as points in that *n*-dimensional vector space, where *n* is the number of variables.

Data matrix					
	Variable #				
	1	2	3	⋮	<i>K</i>
Sample #1	<i>x</i> ₁₁	<i>x</i> ₁₂	<i>x</i> ₁₃	⋮	<i>x</i> _{1<i>K</i>}
2	<i>x</i> ₂₁	⋮			<i>x</i> _{2<i>K</i>}
3	⋮				⋮
⋮	⋮				⋮
⋮	⋮				⋮
<i>N</i>	<i>x</i> _{<i>N</i>1}				<i>x</i> _{<i>NK</i>}
<i>N</i> × <i>K</i>					

Fig. 1. Format of the data matrix, where *N* is the number of samples and *K* is the number of variables.

Rules of matrix algebra can be applied to the manipulation and interpretation of data in this type of matrix format. One of the most basic operations that can be performed is to plot the samples in variable-by-variable plots. When the number of variables is as small as two then it is a simple and familiar matter to construct and analyze the plot. But if the number of variables exceeds two or three, it is obviously impractical to try to interpret the data using simple bivariate plots. Pattern recognition provides computer tools far superior to bivariate plots for understanding the data structure in the *n*-dimensional vector space.

Many of the tools are aimed at classification and prediction problems, such as the handwriting example, where a training set of data vectors for which the property is known is used to develop a classification rule. Then the rule can be applied to a test set of data vectors for which the property is

unknown. Other pattern recognition methods allow the viewing of two-dimensional projections of higher dimensional data structure. Still other methods apply a mathematical procedure to uncover intrinsic grouping of data points in four or more dimensions (hyperspace).

Throughout the 1970s, applications of pattern recognition were found in the chemical sciences. Other methods of multivariate mathematics and statistics were borrowed or invented, and a new discipline called chemometrics arose. In 1974, the Chemometrics Society was formed, and the first Chemometrics newsletter came out in 1976 (12).

By about 1980, as advances in computing technology were rapidly expanding the ability of analytical instruments to collect and process data, a new emphasis in chemometrics was emerging. With computers interfaced to spectroscopic instruments, it became possible to collect hundreds of channels of information, ie, to collect intensities at hundreds of wavelengths, creating a data vector of equivalent dimension. That, added to the fact that automated sample handling techniques created a higher sample throughput, resulted in the capability to create large data matrices. By placing aspects of the analytical instrument under computer control and applying chemometrics, it became possible to improve the optimization, resolution, calibration, and other operating parameters in what began to be called intelligent analytical instrumentation (13) (see ANALYTICAL METHODS, TRENDS).

It was recognized that pattern recognition techniques along with other related multivariate methods of mathematics and statistics have much to offer the entire chemical analytical process as shown schematically in Figure 2. This scheme has become the framework for the development of new techniques in the field of chemometrics. Thus the emphasis during the 1970s on applications of pattern recognition to chemical data interpretation was joined by a growing focus during the 1980s on the application of multivariate methods to analytical method development.

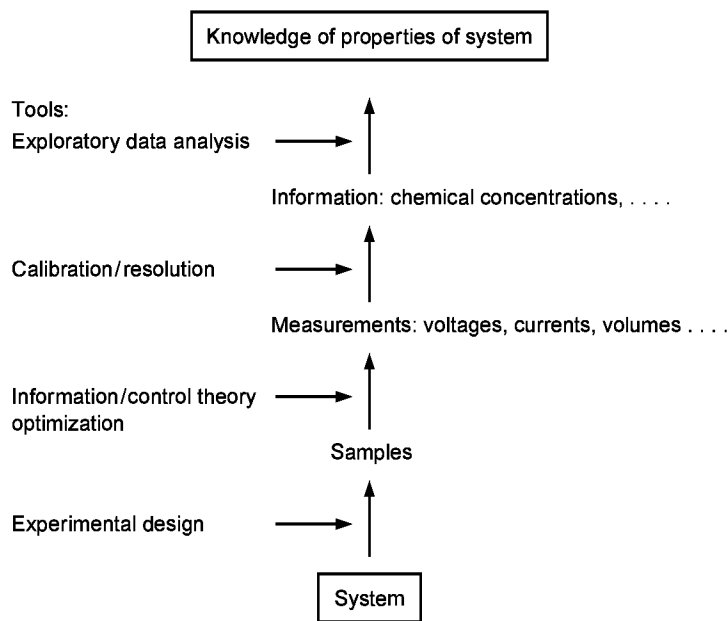


Fig. 2. Chemometrics tools and the analytical approach.

This approach corresponds to the steps of the analytical process in Figure 2. Whereas the last step in a practical problem is the extraction of knowledge about the properties of the system from a large data matrix of chemical information, it is the starting point of this discussion of chemometrics methods. One usually begins by taking samples from a system, applying some method to the samples to obtain a signal which is, hopefully, correlated to certain chemical aspects of interest, calibrating the technique to permit quantitative estimation of chemical concentrations or other parameters, and then after the data are assembled, applying methods to interpret the significance of the data. This discussion is presented in the opposite order because many of the fundamentals of pattern recognition and multivariate data analysis facilitate understanding of the calibration, signal resolution, and other methods of chemometrics. It also corresponds to the chronological development of the field.

Exploratory Data Analysis

Basic Assumptions of Pattern Recognition. Given a k -dimensional data set, that is, a set of samples with k measurements made on each sample, the goal is to learn something about a property or behavior, answer a question, or test a hypothesis about the system. The type of property or question to be investigated influences the selection of data analysis techniques that are appropriate to use. Generally, data analysis problems are one of two types involving either category data or continuous property data. A continuous property is a dependent variable associated with a sample that has a continuous range of possible values. A familiar example of a data analysis technique appropriate for this would be multivariate linear regression where the continuous property, the dependent variable, is related to a set of measurements, the independent variables. A category is a designated group of samples. Categories that are entirely independent of one another are discrete categories; those with some dependence on one another, such as low, middle, and high, are called continuous categories. Note that samples can be a wide range of objects, and they may be classified in any way depending on the property of interest. The same set of samples may be grouped in more than one way. In category-type data analysis, the property of interest about the system relates to the category membership of the data, which is obviously not amenable to the regression approach as used for continuous properties. Pattern recognition is especially designed for category data analysis problems.

There are four main categories of pattern recognition techniques as illustrated in Figure 3: preprocessing, display, unsupervised learning, and supervised learning. Preprocessing techniques are utilized to ensure that the form or representation of the data is conformable with the pattern recognition algorithms. They are designed to transform the data into the most informative representation in the context of the study. The data analyst may then choose to display the data in two or three dimensions for human inspection while preserving the maximum amount of information about data structure in the k -dimensional space. Unsupervised learning refers to methods that make no *a priori* assumptions about category-membership of the samples. They are used in uncovering intrinsic clusters or other patterns in the data. Conversely, in supervised learning the computer learns to classify the samples based on *a priori* knowledge about their category designation. The goal is to develop an optimal classification rule in order to test the validity of a hypothesis or classify an unknown sample.

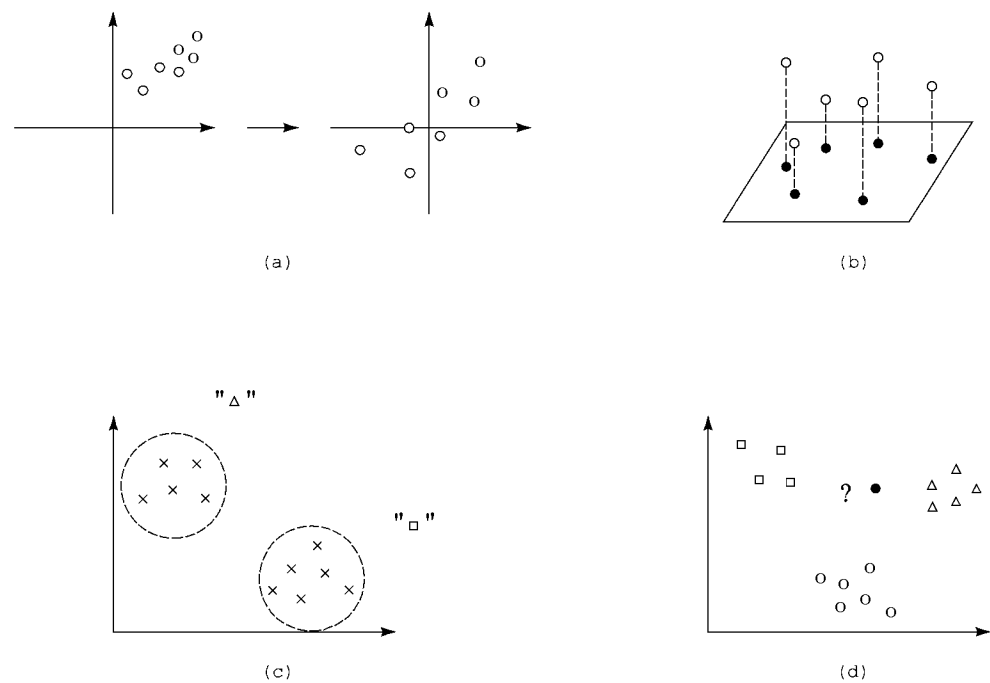


Fig. 3. Types of pattern recognition techniques: (a) preprocessing, (b) display, (c) unsupervised learning, and (d) supervised learning.

The successful application of pattern recognition methods depends on a number of assumptions (14). Obviously, there must be multiple samples from a system with multiple measurements consistently made on each sample. For many techniques the system should be overdetermined; the ratio of number of samples to number of measurements should be at least three. These techniques assume that the nearness of points in hyperspace faithfully reflects the similarity of the properties of the samples. The data should be arranged in a data matrix with one row per sample, and the entries of each row should be the measurements made on the sample, as shown in Figure 1. The information needed to answer the questions must be implicitly contained in that data matrix, and the data representation must be conformable with the pattern recognition algorithms used.

Preprocessing Techniques. Preprocessing refers to any transformation of the original data. After a transformation, a variable is called a feature to distinguish it from the original variable. Examples of preprocessing techniques run the gamut from scalar multiplication to logarithmic transformation and rotation.

The first issue in preprocessing is to fill in missing data by an appropriate means. This is necessary in order to plot all points in the same k -dimensional coordinate system. Common methods include the mean fill, principal component fill, and the random fill methods (14). Regardless of the method used, filling in missing data alters the data structure, which represents a limitation to the success of pattern recognition algorithms. Redundant or constant variables should also be detected and eliminated in the preprocessing phase by examining the correlation matrix for high coefficients of correlation.

The purpose of translation is to change the position of the data with respect to the coordinate axes. Usually, the data are translated such that the origin coincides with the mean of the data set. Thus, to mean-center the data, let x_{ik} be the datum associated with the k th measurement on the i th sample. The mean-centered value x'_{ik} is computed as $x'_{ik} = x_{ik} - \bar{x}_k$ where $\bar{x}_k$ is the mean for variable k . This procedure is performed on all of the data to produce a new data matrix X' the variables of which are now referred to as features.

Normalization is a preprocessing method often applied to spectral data. It makes the lengths of all of the data vectors the same. Thus the sum of the squares of the elements of the data vectors is constant for all samples in the set. If c_i is this sum for the unnormalized sample i , then to normalize the data vectors to the constant m , each element of the data vector would be multiplied by $m/\sqrt{c_i}$. A common example of this method is normalizing the area under a set of curves to unit area. Application of this method effectively removes the variance in a data set because of arbitrary differences in magnitudes of a set of measurements when such variation is not meaningful and would obscure the significant variance.

Scaling methods are applied in preprocessing in order to remove any inadvertent weighting of variables that arise because of arbitrary units of measure (1,14). When variables are scaled, they are put on an equal footing with one another in terms of some criterion, usually range or variance. Range scaling is performed by placing the minimum value of each variable at the origin and dividing each datum by the range of the data so that the maximum value of each new feature is 1.0. Autoscaling offers the advantage that it removes inadvertent weighting that arises because of arbitrary units but is less sensitive to outliers than range scaling. Autoscaling to unit variance is performed by mean-centering and dividing by the standard deviation s_k :

$$x'_{ik} = \frac{x_{ik} - \bar{x}_k}{s_k} \tag{1}$$

where s_k is the standard deviation of variable k :

$$s_k = \left[\frac{1}{(N-1)} \sum_{i=1}^N (x_{ik} - \bar{x}_k)^2 \right]^{1/2}$$

Feature weighting, by contrast, is used to give certain variables more influence in a problem. Instead of putting the variables all on an equal footing, it is used to stretch, or emphasize, certain axes (variables). The purpose of feature weighting is to provide an index w_k of the ability of a variable to discriminate between samples on the basis of category membership, and then to improve classification results by scaling each axis by its weight w_k . Feature weighting is of great utility in a classification problem because it can reveal whether or not a set of measurements actually contains information relevant to the problem, and if so, which subset of measurements is necessary and sufficient to do the job (14).

The frequency histogram with respect to a feature x_k of two categories, I and II, is given in Figure 4. An expression for how well this feature separates the two curves can be derived. A very discriminating feature yields widely separated distributions; conversely, the distributions are very nearly superimposed for a poor one. The variance weight for these categories, w_k (I,II), is calculated as the ratio of the intercategory variances to the sum of the intracategory variances (14). The variance weight is always greater than or equal to 1.0 units of variance even if one or more features have no discriminating ability. The Fisher weight is similar to the variance weight except that it uses the difference between category means instead of the intercategory variances. The Fisher weight may therefore go to zero for a nondiscriminating feature, if the means are identical. In chemical applications, either the Fisher or variance weights would be calculated and the axes scaled by these values to produce a new set of features x'_{ik} :

$$x'_{ik} = w_k x_{ik}$$

(2)

The values of the weights depend on the classification objectives of the problem. Weights can be recalculated as new hypotheses or category assignments are posed during the course of the study.

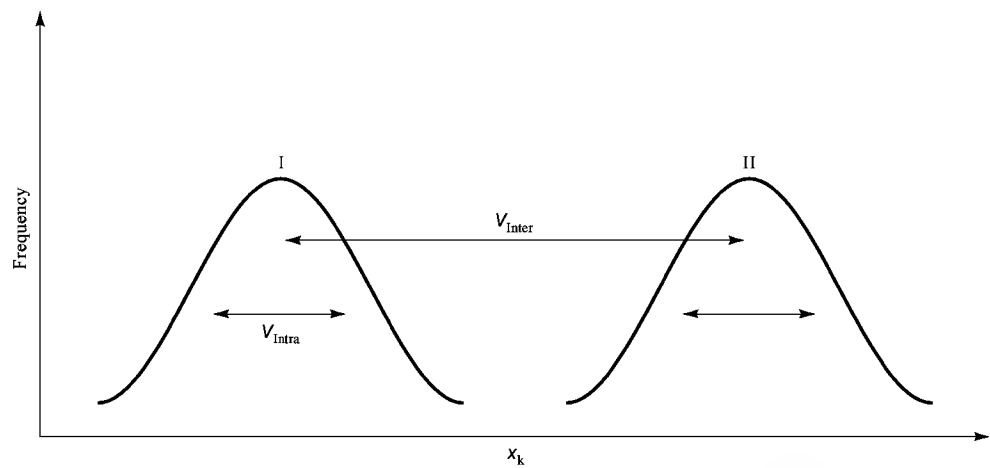


Fig. 4. Frequency histogram of data in categories I and II for variable x_k where V = variance (14).

Preprocessing methods of rotation shift the orientation of the data points with respect to the coordinate axes by some angle θ (Fig. 5). The operation is performed mathematically by applying a rotation matrix R to the original data matrix X to obtain the coordinates of the points with respect to Y , the new axes:

$$Y = XR$$

(3)

x and y are data matrices in row format, ie, the samples correspond to rows and the variables to columns. Some mathematical literature uses column vectors and matrices and thus would represent this equation as $Y = R^T X$. The purpose of rotation in general is to find an orientation of the points that results in enhanced understanding of the underlying chemical behavior of the system.

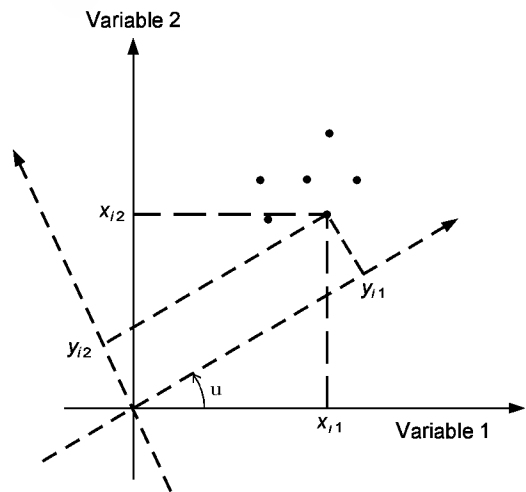


Fig. 5. Rotation of coordinate axis where $y = XR$ and R is a rotation matrix. Coordinates x_i refer to sample i in the original reference system; y_i to the new rotated system.

Eigenvector rotation is used as a preprocessing step in preparation for display and unsupervised learning. The method rotates the coordinate axes through a special angle, one such that the first new axis corresponds to the direction of greatest variance, spread, in the data structure, and each successive axis represents the maximum residual variance (Fig. 6). Mathematically, the rotation matrix R and new data coordinates Y are determined by diagonalizing the correlation matrix associated with X , yielding the eigenvalues λ , and the eigenvectors which comprise R . Detailed mathematical treatment of the process and related methods can be found (1,10,15,16). The eigenvectors defining the new coordinate system are each linear combinations of all of the original variables. The eigenvector coefficients, or loadings, are the elements of each eigenvector, and reveal the correlation of the eigenvector to each original vector. By analyzing the loadings, one can determine which original variables have the highest weight, ie, influence in determining the direction of the eigenvector. This information can be used to attribute a physical or chemical significance to the eigenvector. The new coordinates of the points in the eigenvector coordinate system, Y , are called the scores. The scores can be plotted in bivariate plots, for example a plot of eigenvector 1 versus eigenvector 2. The resulting plot allows viewing of a projection of the data onto two dimensions, but because these two eigenvectors are linear combinations of all of the original variables, much more information is being viewed than in a bivariate plot of two original variables.

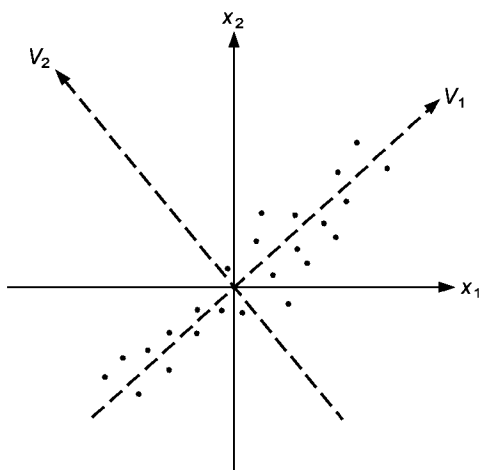


Fig. 6. Eigenvector rotation. The first eigenvector V_1 spans the direction of greatest variance in the data. x_1 and x_2 represent the two original variables.

The eigenvectors are computed such that the first vector spans the direction of largest variance, and each successive vector spans the maximum residual variance. The magnitude of the eigenvalue λ_k of each vector reflects what percentage of the total variance in the data set is represented by that vector. Usually in practice, the first few eigenvectors represent proportionally more variance than the last few, which often represent noise or other minor fluctuations. One can calculate the percentage of variance retained in any subset α eigenvectors of the total N eigenvectors as

$$\% \text{ variance} = \frac{\sum_{k=1}^{\alpha} \lambda_k}{\sum_{k=1}^N \lambda_k} \times 100 \tag{4}$$

Thus, for example, if there were five original variables, and therefore five eigenvectors computed, with eigenvalues found to be

λ_1	2.1
λ_2	1.8
λ_3	0.6
λ_4	0.3
λ_5	0.2

then a plot of eigenvector 1 versus eigenvector 2 would contain $\frac{2.1+1.8}{5} \times 100 = 78\%$ of the information contained in the entire data matrix. Furthermore, in a hypothetical example, if the loadings of just eigenvector 1 are found to be

Variable k	Loading in eigenvector 1	
1		0.865
2	0.121	
3		1.511
4	0.108	
5	0.023	

one can select the variables corresponding to the loadings of the highest absolute value. The two largest are 1.511, 0.865, corresponding to variables 3 and 1, respectively. The remaining loadings are markedly smaller in absolute value. After observing that variables 3 and 1 are highly correlated to eigenvector 1, the chemical or physical measurements corresponding to those variables would be examined to see if there was a pattern of association or other significance that could be attributed to the combination of variables 3 and 1. These three variables covary, that is, vary together, and may be the telltale fingerprint of an underlying natural process or factor that is influencing the system.

Besides analyzing the loadings, it is usually of interest to determine the intrinsic dimensionability of the data set. By applying statistical criteria, the number of statistically significant eigenvectors can be determined, ie, the ones that contain meaningful information, as distinguished from those that represent noise. It also provides a means of data reduction, that is, the discarding of factors that do not contain significant information about the data. As a preprocessing method, performing eigenvector rotation can result in a signal-to-noise enhancement. Ideally, the chemical information is contained in the first one or more eigenvectors having the largest variances, and the noise contained in the eigenvectors of smallest eigenvalue may be discarded.

The eigenvectors are linear combinations of all of the original variables. Thus a linear relationship is assumed to exist between the variables and the underlying factors governing the data structure. If these relationships are instead nonlinear, eigenanalysis may give some small indication of this but cannot be used to uncover the underlying factors. A number of techniques have been devised for the nonlinear case such as nonlinear least squares, multidimensional scaling, and parametric mapping (17–19). To visualize how the nonlinear projection methods work, imagine a set of data points lying along a curved line in two dimensions as depicted in Figure 7 (19). Analyzed by linear principal component analysis, the data would yield two factors even though there is only one underlying nonlinear independent variable.

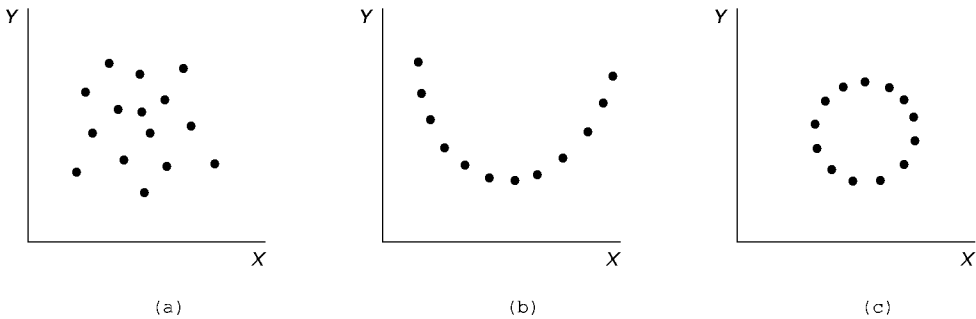


Fig. 7. Results of linear and nonlinear methods for analyzing the underlying structure of some data sets: (a) data points randomly distributed; (b) data points on a curved line; and (c) data points on a circle correspond to Datasets I, II, and III, respectively. Dimensionality was found by dataset, principal component analysis, multidimensional scaling, and parametric mapping (19).

The choice of which of the many preprocessing methods to apply depends on the type of data involved and the context and objectives of the problem. The importance of appropriate preprocessing cannot be overemphasized; improper treatment of the data at this stage may make the rest of the analysis meaningless.

Display Methods. Display methods refer to techniques of plotting k -dimensional data in two or three dimensions. Methods of displaying the data are very important because these allow the human pattern recognizer to analyze the data. Furthermore, they provide a way to oversee the application of other pattern recognition algorithms. Displaying the data allows spot checking for outliers, errors in data entry, or other unusual or inconsistent behavior. Accordingly, it is a useful validation step before further algorithms are applied, as well as afterward to interpret and validate results. Linear methods of display are called projections (10,14). The axes in such cases are linear combinations of the original variables. Eigenvector rotation followed by plotting the scores is perhaps the most frequently used method if displaying multivariate data in chemometrics applications. Nonlinear display methods are called mappings (10,14). Mappings involve coordinate axes which are nonlinear combinations of the original variables. One such method called nonlinear mapping (NLM) (9,10,20), takes the eigenvector plot as a starting point and then iteratively adjusts the scores so as to find the best two-dimensional representation that optimally preserves the n -space interpoint distances.

The use of eigenvector rotation and variance weights for preprocessing and display is illustrated by an example from clinical chemistry involving the differential diagnosis of liver diseases (21,22) which, based on only one or two blood enzymes, is very difficult. A plot of two enzymes for 55 patients having liver diseases A and B, or unknown diagnosis X, is shown in Figure 8a. There is insufficient information in this bivariate plot to distinguish unambiguously between these two diseases. When six additional blood enzymes were measured, an eigenvector rotation of the eight-dimensional data set yielded a greater separation between diseases A and B. As shown in Figure 8b, a plot of eigenvector 1 versus 2 retained 65% of the total variance in the data set, and revealed a clearer separation between categories. Application of variance weights showed which enzymes were most useful for distinguishing between diseases A and B: alkaline phosphatase, which had a weight of 3.5, was the most discriminating variable, followed by glutamate pyruvate transaminase and guanine deaminase at 1.8. The eigenvector plot of the variance weighted data, obtained after applying the variance weights to all of the variables, showed even greater separation between categories (Fig. 8c).

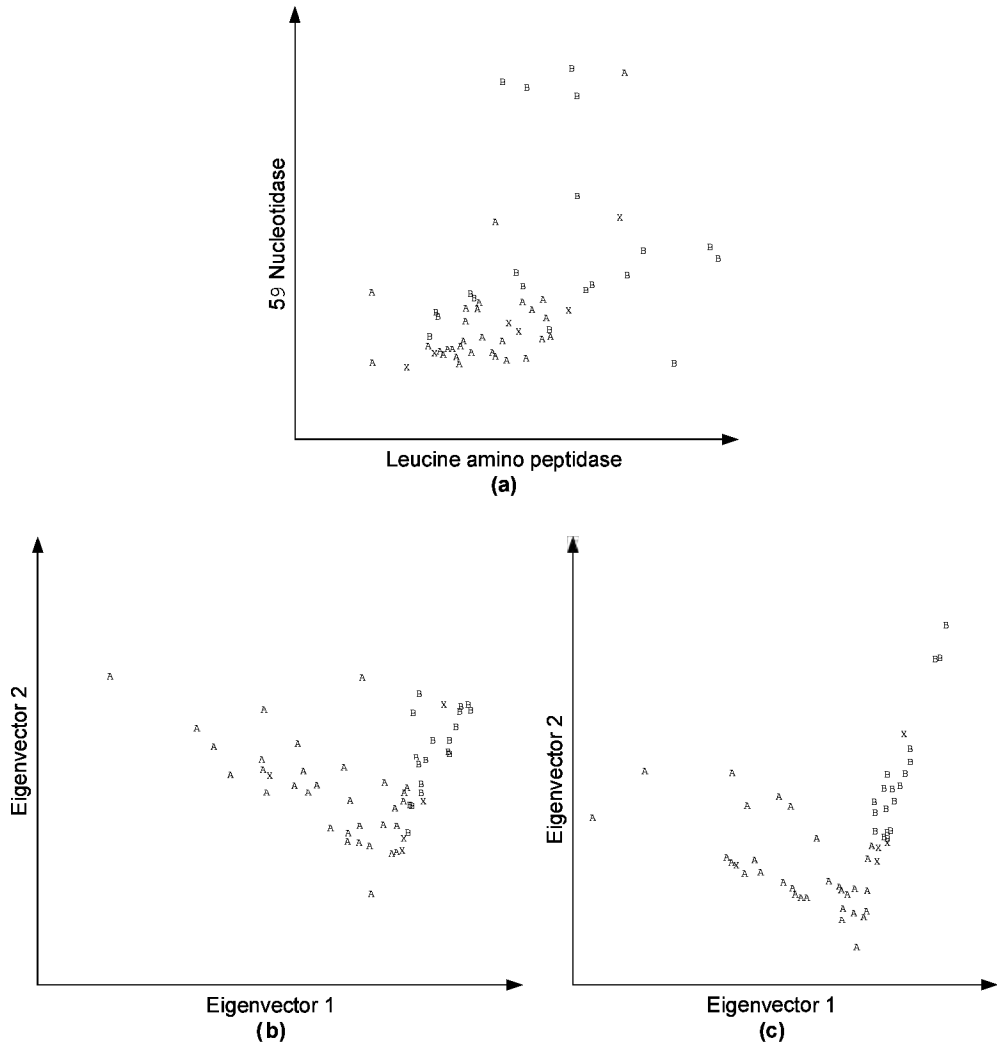


Fig. 8. Plot of data from patients having liver diseases A or B or unknown X: (a) on two blood enzymes; (b) scores of points on the first two eigenvectors obtained from an eight-dimensional enzyme space; and (c) eigenvector plot of the variance weighted data. Variance weights ranged from 3.5 to 1.2 for the eight blood enzymes measured. A weight of 1.0 indicates no discrimination information (22).

One newer application of eigenvector rotation in display is in multivariate statistical process control (MSPC) (23). In a manufacturing process, plant operators often must monitor many conditions and operating parameters to ensure that the process remains within normal and safe limits (see PROCESS CONTROL). However, monitoring many univariate displays has the same disadvantages as for univariate plots: there are too many, and they are not informative enough. By monitoring eigenvector plots instead, one can monitor a great amount of information in one plot and ensure that the manufacturing process remains within its n -dimensional specification space.

Unsupervised Learning. The objective of unsupervised learning is to uncover intrinsic structure or underlying behavior of a data set without making *a priori* assumptions about the data (Fig. 3c). It can be thought of as a hypothesis-generating activity. It is also used to check the validity of data and to detect outliers or strange or faulty results. The most basic unsupervised learning is done by the scientist when inspecting the data using a suitable display technique as described. Most other unsupervised learning techniques are based on finding clusters of points in the data. Points are grouped together based on their nearness or similarity into clusters. The method assumes that the nearness of points in hyperspace reflects the similarity of their properties.

In a typical application of hierarchical cluster analysis, measurements are made on the samples and used to calculate interpoint distances using an appropriate distance metric. The general distance, d_p , is given by

$$d_{ij} = \left[\sum_{k=1}^K (x_{ik} - x_{jk})^n \right]^{1/n}$$

(5)

For $n = 2$, this is the familiar n -space Euclidean distance. Similarity values, S_{ij} , are calculated as

$$S_{ij} = 1 - \frac{d_{ij}}{d_{ij(\max)}} \tag{6}$$

where d_{ij} is the distance between points i and j , and $d_{ij}(\max)$ is the largest distance in the distance matrix. In this way, the two most distant points in the data set have $S = 0.0$ and identical points would have the maximum similarity of 1.0.

In one implementation of hierarchical cluster analysis, each point is initially assumed to be a lone cluster. The similarity matrix is scanned for the largest value, the corresponding points of which are clustered together and treated as a single point. The respective rows and columns of the old points are deleted and the new cluster is added as the average of the two points. This process is repeated until all the points have formed one single cluster. The result of this procedure is a diagram called a connection dendrogram which can be analyzed for clusters. A schematic illustration of clustering and a corresponding dendrogram is shown in Figure 9. The dendrogram does not automatically make cluster assignments, but rather is an aid to learning something about the data. Clusters may be assigned by a scientist, or they may be assigned by a criteria imposed on the algorithm, such as a preset number of clusters, or when the change in similarity coefficient needed to form the cluster exceeds a certain value. Whatever criteria are used to establish cluster assignment, the next step is then to analyze the chemical or physical significance of the data structure.

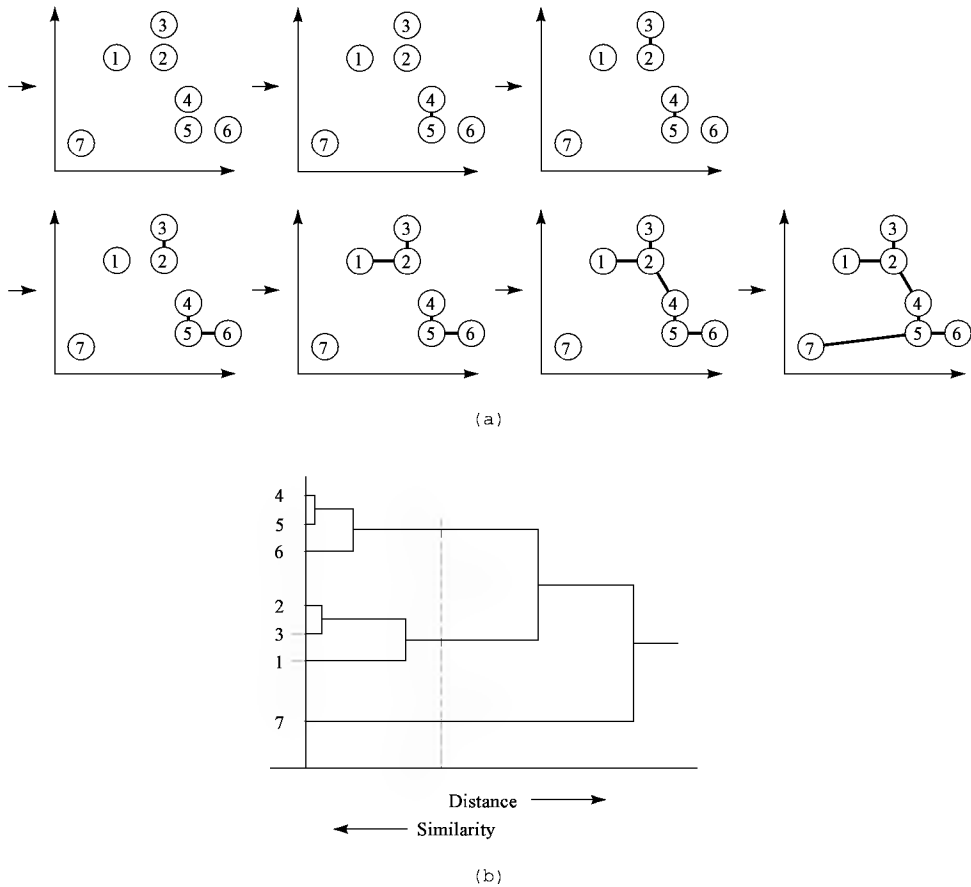


Fig. 9. (a) Single-link clustering process and (b) corresponding connection dendrogram (14). Reprinted with permission.

In R-mode cluster analysis, the clustering is performed on the transpose of the data matrix. Such a procedure yields information about the similarity of the variables (or features) rather than about the samples. The method can be used to complement eigenanalysis in uncovering the underlying factors that govern the data structure. An example of the use of R-mode cluster analysis comes from a study of rainwater chemistry (24). Rainwater samples from various sites in the Pacific Northwest were analyzed for 16 trace metals and ions. Eigenvector rotation of the data suggested that three dominate factors were controlling the chemistry of the rainwater: the sea salt factor brought by prevailing winds, the copper smelter located in the region, and the automobile urban pollution factor (see AIR POLLUTION). The hypothesis that these three factors were the main influences on rainwater chemistry was developed on the basis of the dominant loading (eigenvector coefficients) of each eigenvector. The largest coefficients in the first new coordinate were As, Cu, and Sb; in the second coordinate, Na, Cl, Ca; in the third coordinate, NO₃ and H⁺; corresponding to smelter, sea salt, and automobile exhaust, respectively. Additional evidence to either support or counter this hypothesis can be obtained using R-mode cluster analysis. When the clustering was done on the transposed rainwater data matrix, the resulting dendrogram (Fig. 10) showed an excellent correspondence to the eigenvector results.

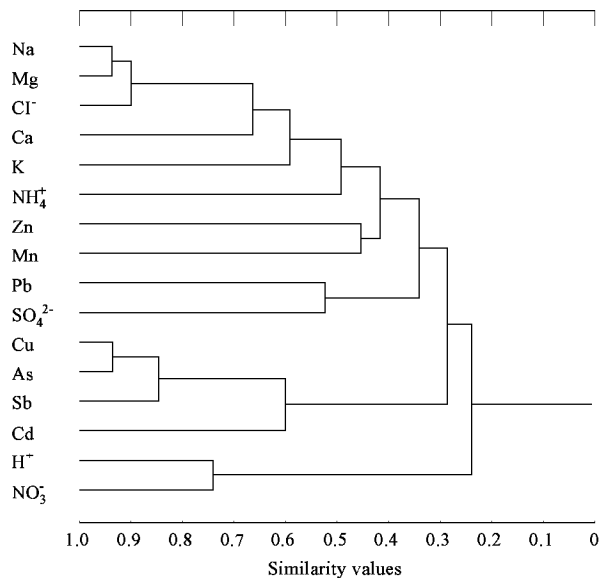


Fig. 10. R-mode cluster analysis of the Pacific Northwest rainwater study (24). Reprinted with permission.

In unsupervised learning, the outcome is usually a hypothesis to then be tested, often using classification or prediction methods. If the unsupervised learning process suggests the presence of distinct clusters, the hypothesis can be tested by applying a classification method to the data. A low number of misclassified samples would tend to reinforce the hypothesis.

Supervised Learning. Supervised learning refers to a collection of techniques in which *a priori* knowledge about the category membership of a set of samples is used to develop a classification rule. The purpose of the rule is usually to predict the category membership for new samples. Sometimes the objective is simply to test the classification hypothesis by evaluating the performance of the rule on the data set.

The classification rule is developed on a training set of samples with known category memberships. An evaluation set is used to rate the performance of the rule by comparing the category predictions with the true classifications. A test set is comprised of data vectors the true categories of which are unknown. Usually, a study begins with just a training set and how to reserve some of the samples for an evaluation set must be decided. In one approach, called the leave-one-out procedure, each of *N* initial data vectors is removed one at a time to be used as an evaluation set while the *N* - 1 vectors remaining are used as the training set. The rule is trained and evaluated a total of *N* times. If the training set has been selected carefully, then the average performance is a good estimate of the real performance of the classification rule. If the rule is accurate for the training set, then the information needed for classification is indeed contained in the data matrix. If it is not accurate, then other measurements should be included in the analysis. If the rule is predictive for an evaluation set, then the training set is probably a representative sampling of the system. Conversely, a low predictive ability indicates that more samples should be taken.

The first applications of pattern recognition in chemistry involved the use of the linear learning machine (LLM) to interpret spectroscopic data (5,9). The linear learning machine uses a linear discriminant function as the basis for classification. A linear discriminant function is a linear function pertaining to a boundary that divides the *n*-dimensional space into category regions and can be used to make a prediction of category membership for test samples (Fig. 11) (14). One disadvantage is that the classification boundary determined by the algorithm is nonunique. That is, unknowns may be classified differently depending on the order the training set vectors were presented to the LLM. Another disadvantage is that it fails for linearly nonseparable data, such as curved or concentric data structures.

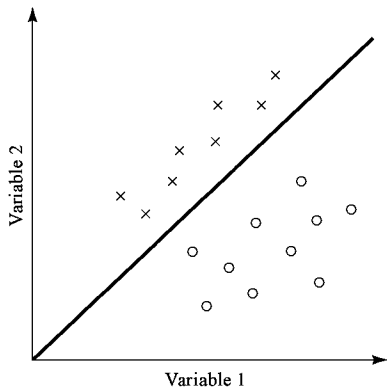


Fig. 11. Linear discriminant function defines the boundary between two categories.

The *K*-nearest neighbor (KNN) technique (9,14) is a classification method in which an unknown is classified according to the majority vote of its *K*-nearest neighbors in the training set in *n*-dimensional space. Should there be a tie, the closer neighbors are given greater weight. Nearness is measured using an appropriate distance metric as discussed in the section on unsupervised learning. The KNN rule has several advantages over the linear learning machine. First, it is a multicategory classifier. Secondly, its performance is not limited by the distribution of data points to the degree that LLM is. Bimodal data distributions within a category or even more unusual data structure does not hamper the use of KNN. Furthermore, KNN generates unique solutions; the classification results do not depend on the order in which data are fed to the computer.

A priori, it is not known which variables are useful in a classification problem. It is always advisable to measure many things at first and then determine the most discriminating variables by means of the feature weights. A further use of feature weighting is feature selection: to select an optimal set of features that are necessary and sufficient to solve the classification problem, based on the feature weights and the intervariable correlations. Feature selection saves time and reduces costs, both for the chemical analysis as well as for information acquisition, storage, and processing, and can increase the ease and efficiency of the classification procedure. Feature selection can also lead to an understanding of the essential features that play important roles in the chemistry of the system. Moreover, it provides important feedback to the experimental design. Feature selection procedures can reveal which measurements are discriminating and which are not. Even negative results are extremely important.

An example of a classification problem in which feature weighting and selection was important comes from forensic chemistry (qv). A classification method was needed to determine the paper grade and manufacturer of a paper scrap found at the scene of a crime. In this study, 119 sheets of paper (qv) representing 40 different paper grades and nine manufacturers were obtained (25). The objects were then the paper samples, and the variables consisted of

13 elements measured by neutron activation analysis. The data were autoscaled and the variance and Fisher weights were calculated using the paper grades as the categories, and then using manufacturers as the categories. The weights are presented in Table 1. As shown in the table, Al is an extremely discriminating variable for paper grade and is somewhat discriminating for manufacturers. The weights show that the measurements made do contain information needed to classify paper samples and which variables are most efficient for this purpose.

Table 1. Variance and Fisher Weights in the Forensic Paper Study^a

Element	Paper grade		Manufacturer	
	Variance	Fisher	Variance	Fisher
Na	7.39	6.62	1.49	0.048
Al	66.95	22240.0	3.03	0.650
Cl	9.96	137.1	1.67	0.085
Ca	13.24	11.08	1.98	0.141
Ti	17.94	12.78	1.66	0.092
Cr	8.67	41.53	1.75	0.106
Mn	13.01	15.43	2.37	0.182
Zn	4.87	18.24	1.99	0.163
Sb	10.19	31.68	1.92	0.138
Ta	2.06	1.71	1.25	0.013

^a Ref. 25.

Classification problems in chemistry often involve the prediction of the source of a material, or its type, grade, or quality. For example, classification methods have been used to detect counterfeit whiskeys (26). The need for such a forensic method arises when a bottle of well-known, high quality liquor is filled with less expensive, low quality product, a crime under Federal law (see BEVERAGE SPIRITS, DISTILLED). The problem was solved using gas chromatography (gc) in concert with pattern recognition. A training set of 34 commercially available brands of Scotch whisky were obtained as were chromatograms on material fresh from the bottle and after exposure to air for a period of time. Seventeen gc peaks were selected as the variables. Data were autoscaled, Fisher and variance weights calculated, and KNN performed. Isoamyl alcohol and acetaldehyde were found to be the two most discriminating variables between Chivas and non-Chivas brands. The training set provided perfect classification results for these two categories.

Classification methods have been used in several studies in geochemistry and archeology. The most frequently cited is the problem of tracing the source of obsidian glass used in arrowheads (27). A detailed description of the pattern recognition approach used is available (14). Similar problems, identifying the source or quality of a material, can arise in virtually all fields of technology. For example, pattern recognition methods combined with pyrolysis—gas chromatography have been used to classify fungi (28).

Often the goal of a data analysis problem requires more than simple classification of samples into known categories. It is very often desirable to have a means to detect outliers and to derive an estimate of the level of confidence in a classification result. These are things that go beyond strictly nonparametric pattern recognition procedures. Also of interest is the ability to empirically model each category so that it is possible to make quantitative correlations and predictions with external continuous properties. As a result, a modeling and classification method called SIMCA has been developed to provide these capabilities (29–31).

In the SIMCA method, a principal component model is fit to each category separately, and statistical confidence envelopes, ie, volumes or hypervolumes, are constructed around the model to contain the data points. The number of principal components used in the model may be preselected or determined by cross-validation. If one principal component is used, the data are modeled by the class mean and a line, the first principal component. If two principal components are used, the class mean and a plane form the model. These models are schematically depicted in Figure 12. After the categories have been fit with principal component models, SIMCA can be used to classify test points. For a test data vector x_i , the scores of x_i are calculated for each of the category models. Then, by examining the residual variance of x_i to each of the models, the one with the best fit or least residual variance can be identified. When the residual variance of x_i to a category model is less than or of the same order as known members of that category, then x_i is likely to belong to that category. Conversely, if it is much larger than the known category members, it is judged not to belong to that category.

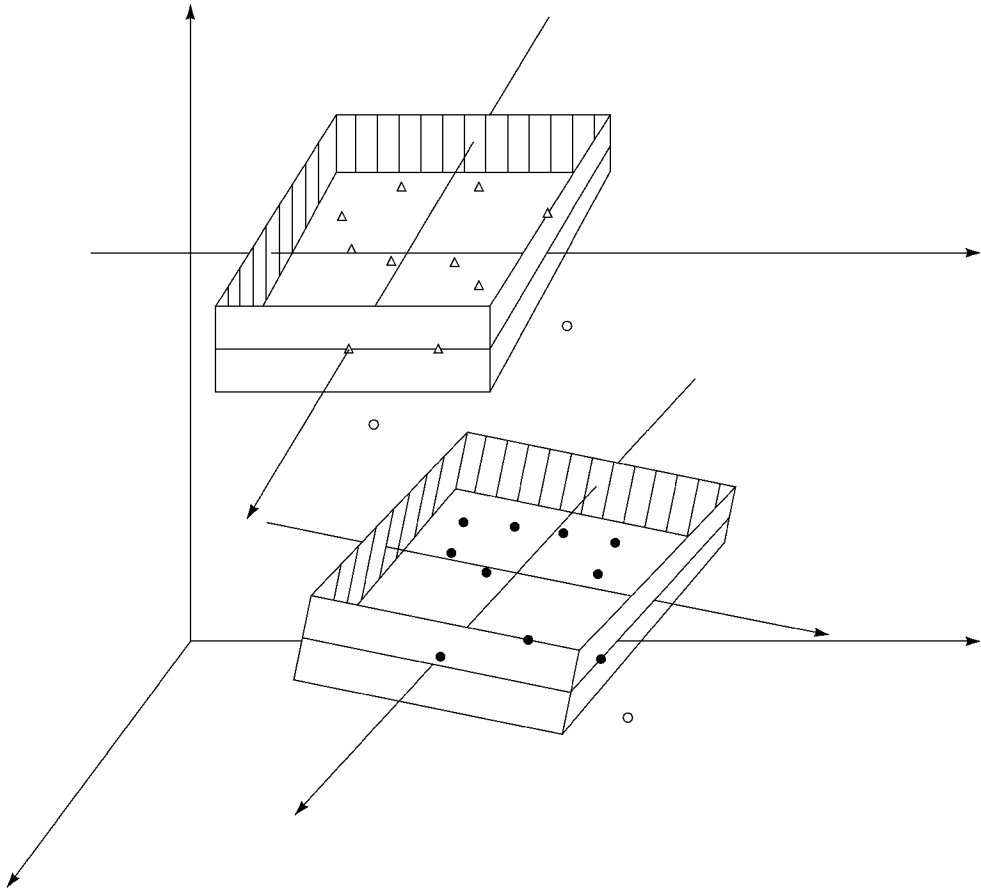


Fig. 12. SIMCA class models.

This kind of statistical consideration is used to detect outliers, ie, when a sample does not belong to any known group. It is also the basis of a variation of SIMCA called asymmetric classification, where only one category is modelable and distinguished from all others, which spread randomly through hyperspace. This type of problem is commonly encountered in materials science, product quality, and structure–activity studies.

The application of SIMCA to problems in chemistry can be divided into four basic types according to the level and scope of the study (31): level 1 corresponds to simple classification into predefined categories; level 2 has two components, 2-O is level 1 plus outlier detection, and 2-A, is the asymmetric case; level 3 is level 2 plus prediction of one external property; and level 4 is level 2 plus prediction of more than one external property. After covering levels 1 and 2 and proceeding to level 3, it is often desirable to be able to relate the value of an external property to the measurements made on the samples. Many structure–activity studies try to relate a numerical value of biological activity to the structural features and molecular parameters used to describe each sample. A level 3 analysis would accomplish this through multiple regression of the external property on the scores of the data points in a category. A level 4 analysis involves the prediction of several external properties. First, closed class envelopes are constructed for a category in the measurement space and in the property space which may be considered as simply an additional measurement space. Then a direction in each class of the measurement space is obtained such that it is maximally correlated to a direction in property space. The method of path modeling by partial least squares (PLS) can be used to relate external properties to a set of measurements on a data set. The PLS methods will be discussed later.

A number of situations arise in which it is desirable to determine the number of statistically significant eigenvectors. The method of cross-validation is used to calculate these based on a criterion of best predictive ability. In this method the minimum number of eigenvectors needed to span the meaningful variance is determined. Cross-validation is performed by an iterative procedure in which elements are first removed from the data matrix; some percentage γ , often 10%, of the data is deleted in a prescribed manner. Beginning the iteration with the number of principal components N equal to one, a principal component analysis is performed on the reduced data set to extract N components. Then the deleted data values are predicted using these principal components. Using less than the truly significant number of principal components means that the prediction $\hat{x}_{ij}$ incurs an error $e_{ij} = x_{ij} - \hat{x}_{ij}$. These errors are calculated and stored as the same procedure is repeated 100 γ times, changing the deletion pattern position so that each point is left out only once. A quantity called the predictive residual error sum of squares (PRESS) is calculated and plotted for each iteration on N :

$$\text{PRESS}(N) = \sum_i \sum_j e_{ij}^2 \tag{7}$$

The number of components N is incremented by one and the entire procedure is repeated to arrive at a $\text{PRESS}(N + 1)$. In other words, for $N + 1 = 2$, two principal components would be extracted and used to predict the deleted data values. As N approaches the true number of significant components, the prediction should improve, and thus the PRESS should decrease. As the significant number is passed, noise begins to be included within the model, which has low predictive ability. At this point, the PRESS should start to increase again. Thus the basic type of criterion used in cross-validation to select is that when

$$\frac{\text{PRESS}(N + 1)}{\text{PRESS}(N)} > 1 \tag{8}$$

the number of significant principal components is selected as N . When the samples are associated with one or more continuous properties, techniques such as multiple regression, stepwise regression, and canonical correlation can be applied.

Partial least-squares path modeling with latent variables (PLS), a newer, general method of handling regression problems, is finding wide application in chemometrics. This method allows the relations between many blocks of data ie, data matrices, to be characterized (32–36). Linear and multiple regression techniques can be considered special cases of the PLS method.

The advantages of the PLS method are many. First of all, the goal of many studies is to understand the interrelationships between several parts of a large, complex system. Examples that have been studied using PLS include the modeling of a watershed system in which the influence of various sources of water is characterized (37,38) and the way the quality of a chemical product is related to physical process conditions such as temperature, pressure, flow rate, stirring rate, and feedstock (39). In such problems, blocks of data are connected together by some predetermined scheme or causal pathway. The PLS method allows the influence of each block to be evaluated with respect to the path model. Secondly, when the number of variables exceeds the number of samples in a regression problem, stepwise regression can be used, but the variables eliminated may contain useful information, whereas selected variables may have only a spurious correlation. The PLS method allows all of the variables to be retained in the problem by extracting latent variables by an iterative procedure. Latent variables are mutually orthogonal, linear combinations of all the original variables. The power of PLS results from the fact that the latent variables simultaneously describe the maximum predictive variance of a block, and provide maximal fit to the path model. A fundamental assumption made in multiple regression is that the independent variables are truly independent. To the degree that this assumption is invalid, the resulting model parameters are more affected by noise. Attempts to eliminate this collinearity problem have lead to the development of methods such as principal components regression and ridge regression. PLS regression provides a solution because the latent variables derived from the independent variable block are constrained to be orthogonal. Another advantage of the PLS method is the signal-to-noise enhancement gained by using all the measurements. By using only the significant number of latent variables in the procedure, a noise filtering effect is obtained. The simplest type of application is PLS regression where a relationship is sought between a single response or dependent variable. Latent variables T_x are extracted both to model X and to correlate with Y in contrast to principal component analysis, where the latent variables, eigenvectors, only model X .

Calibration Methods

Calibration is an important focus in analytical chemistry. It is the process that relates instrument responses to chemical concentrations. It consists of two basic steps: estimation of the calibration model parameters, and then prediction for new samples of unknown concentration. Calibration refers to the step of the analytical process in Figure 2 where measurements are related to concentrations of chemical species or other chemical information.

In its simplest form, a direct, univariate calibration method proceeds by assuming there is a mathematical model that relates analytical instrument response to concentration. Traditionally in analytical chemistry, the model is assumed to be a linear relation between response r_i and concentration c_i :

$$r_i = kc_i + b \tag{9}$$

where i represents sample number. The slope k and intercept b of the calibration line are commonly estimated using linear regression by least squares using data from a set of standards having known concentrations of the analyte of interest. This is the model for an ideal world, where the analytical sensor is not affected by interfering components in the sample and where the sample matrix itself does not affect the response. In reality, however, the relationship may be nonlinear, and there may be significant interference and matrix effects. Advances in analytical chemometrics have been developed to address statistical considerations, multivariate direct, indirect, internal standard, and standard addition calibration. The statistical aspects include new ways to address nonlinear calibration, to estimate confidence limits and detection limits for the nonlinear case, and to derive expressions for quantities such as limits of detection and determination (40–45).

Direct calibration is the common approach where the model that relates response to concentrations is known, except for random deviations. When

the model is unknown, it must be statistically estimated using indirect calibration. Indirect calibration involves first measuring a multiresponse signal from several samples and then determining the concentrations in the sample by some other method. The two sets of data are then used to estimate the unknown model parameters. The internal standard or internal reference method is useful for drift compensation and performance verification. Standard addition calibration is used when matrix effects are a problem. Matrix effects cause the prediction model to change from sample to sample. The standard addition method (SAM) is used to counteract matrix effects in univariate cases and the generalized standard addition method (GSAM) extends the approach to the multivariate case.

Standards used to construct a calibration curve must be prepared such that the matrix of the standard is identical to the sample's matrix because the values of the parameters k and b associated with a linear calibration curve are matrix dependent. Many areas of chemical analysis are plagued by matrix effects, and it is often difficult to duplicate the sample matrix when preparing external standards. Because it is desirable to eliminate matrix effects, calibration in the sample matrix itself can be performed. This approach is called the standard addition method (SAM) (14). In this method, the standards are added to the sample matrix and the response of the analyte plus the standard is monitored as a function of the added amount of the standard. The initial response is assumed to be R_0 , and the relationship between the response and the concentration of the analyte is

$$R_0 = kC_0 = k\frac{n_0}{V_0} \tag{10}$$

where n_0 is the initial number of moles in the analyte and V_0 is the initial volume of the sample.

Assuming the model holds, after the i th addition,

$$R_i = k\left[\frac{n_0 + n_i}{V_0 + V_i}\right] \tag{11}$$

where R_i is the response after the i th addition, n_i is the total number of moles added at the i th addition, and V_i is the total volume added at the i th addition.

Equation 11 can be written $Q_i = kn_0 + kn_i$, where $Q_i = R_i(V_0 + V_i)$. Q is often referred to as the volume-corrected response. A plot of Q_i versus n_i yields a straight line with a slope of k and an intercept of kn_0 . The initial number of moles, n_0 , is found by extrapolation. At $Q_i = 0$

$$kn_0 = -kn_i \text{ or } n_0 = -n_i \tag{12}$$

as illustrated in Figure 13.

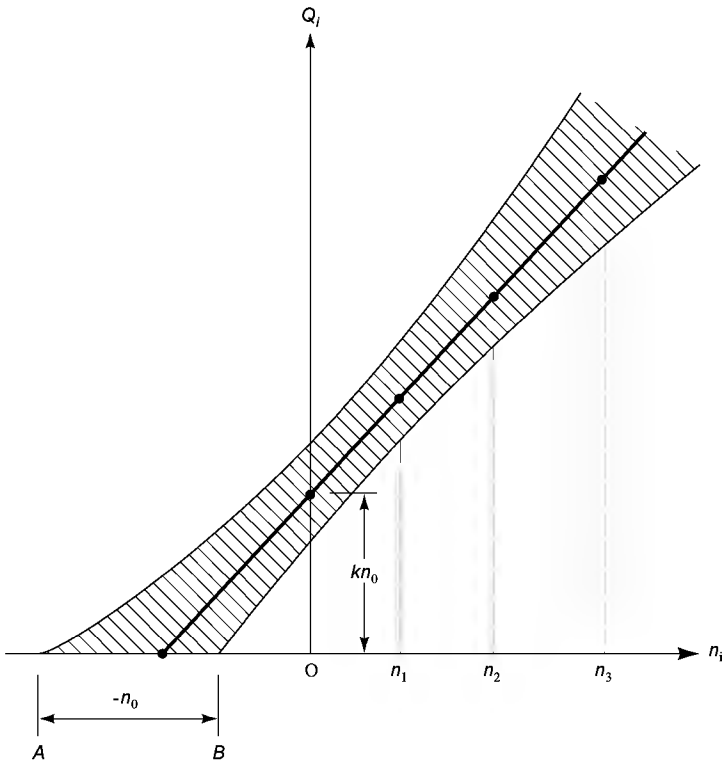


Fig. 13. The standard addition method where AB is the confidence interval for n_0 , the slope of the line $= k$, and $\square$ represents 95% confidence interval (14).

To see how calibration can be extended to multicomponent analysis, the linear model of equation 10 can be generalized to accommodate several analytes in the same sample, and several measurements made on each sample. Expressed in matrix notation, this becomes

$$R_{n,p} = C_{c,r} K_{r,p} \tag{13}$$

where p is the number of sensors, ie, different responses used, r is the number of analytes of interest, n is the number of standard solutions used, and $K_{r,p}$ is the data matrix of linear response constants, the elements of which represent the sensitivity of each sensor to each analyte.

In order for a solution for the systems of equations expressed in equation 11 to exist, the number of sensors must be at least equal to the number of analytes. To proceed, the analyst must first determine the sensitivity factors using external standards, ie, solve equation 11 for K using known C and R . Because concentration C is generally not a square data matrix, equation 11 is solved by the generalized inverse method. K is given by

$$C_s = K - (C^T C)^{-1} C^T R \tag{14}$$

where C^T is the transpose of C , and $(C^T C)^{-1}$ is the inverse of $C^T C$ (assuming it exists). Also, the standard solutions must span the space of analytes and $n > r$.

The matrix $(C^T C)^{-1} C^T$ is called the generalized inverse of C . Having estimated the matrix K , one can then estimate the amounts of analytes in an unknown sample. If the number of sensors is equal to the number of analytes, K is a square matrix. If K^{-1} exists then

$$C_s = R_s K^{-1}$$

(15)

where C_s is the data matrix containing the concentration of analytes in unknown samples and R_s is the data matrix containing the responses obtained for the unknown samples.

If the number of sensors is greater than the number of analytes, then K is *not* a square matrix, and C_s is solved using the generalized inverse of K according to

$$C_s = R_s K^T (K K^T)^{-1}$$

(16)

The generalized inverse method represents another formulation of multilinear least-squares analysis. All the usual assumptions involved with least squares apply.

The sensitivity of the analytical system in the case of multicomponent analysis with a square K matrix may be defined as the absolute value of the determinant of K .

$$\text{sensitivity} = |\det(K)|$$

(17)

where K is a square matrix. When truly specific sensors are used, the K matrix should have nonzero entries along the diagonal and zero entries elsewhere, ie, $k_{ij} = 0$ when $i \neq j$, and $k_{ii} \neq 0$. In other words, each sensor is specific and responds only to one analyte. If any sensor is not specific but only selective, then the appropriate k_{ij} has a finite nonzero value. The more selective the sensor, the smaller the absolute value for this k_{ij} . If interferences are present, it is essential to include them in the calibration process and evaluate their sensitivity factors. Serious errors occur when two interfering analytes A and B are determined without considering the effects one on the other as demonstrated in Figure 14 (14).

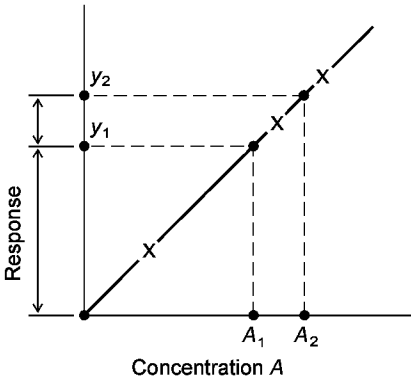


Fig. 14. Errors when two species, A and B , are determined without correction for interference where (x) defines the calibration curve for solutions containing analyte A only; A_1 represents the actual concentration of A ; A_2 the calculated concentration; y_1 represents the response resulting from A_1 ; y_2 represents the observed response; and $y_2 - y_1$ corresponds to the response resulting from the interference of B .

The accuracy of C_s depends on the choice of sensors. As $\det(K)$ increases, the agreement between the calculated C_s and the true C_s gets better. To improve accuracy, it is recommended where possible to have more sensors than analytes. In some cases, such as when one sensor's response is a linear combination of the other sensor responses, the number of sensors must be greater than the number of analytes. If the number of sensors is greater than the numbers of analytes, K is not a square matrix and the sensitivity becomes

$$\text{sensitivity} = |\det(K^T K)|^{1/2}$$

(18)

The method of standard additions can be generalized to include multicomponent analysis. The analyst adds different standards to the sample and estimates C_s from the changes in the responses. The method is referred to as the generalized standard addition method (GSAM) (46,47). Matrix effects are thus eliminated. Figure 15 shows a simple SAM for a case where two analytes give rise to a response on the sensor. The interference caused by the second analyte makes analysis of either analyte impossible. It is therefore necessary to include all interfering analytes in the calibration analysis scheme. Consider the following model to be the true relationships between response and concentration:

$$R_0 = C_0 K$$

(19)

where R_0 is the matrix containing the response of p sensors for n samples, C_0 is the matrix containing the initial concentration of r analytes for each sample, and K is the matrix of sensitivity coefficients (linear response constants).

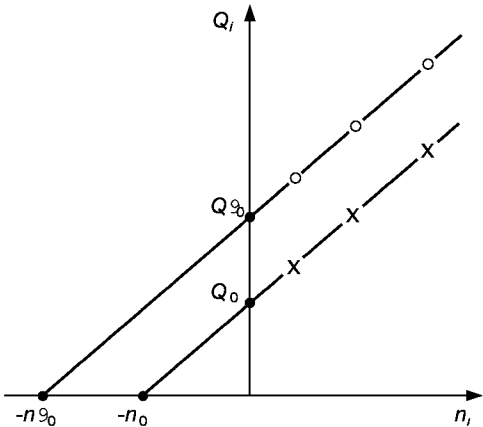


Fig. 15. Effect of interference in an analysis. SAM corrects for matrix but not interference effects where (O) represents the GSAM curve not corrected for

interference, $(\wedge)$ the actual GSAM curve, n'_0 represents a calculated value, Q_0 the true value of Q_0 plus interference, and n_0 the actual value of n .

Multiplying each response and concentration by the initial volume V_0 of the sample, the so-called volume-corrected response equation:

$$Q_0 = N_0 K \tag{20}$$

where Q_0 , the matrix of responses multiplied by the volume of the sample, is obtained, and N_0 is the matrix containing the initial amount in moles, grams, etc of each.

Given that one sample is to be analyzed for r analytes using p sensors ($p > r$) by making a series of n standard additions ($n > r$) to the sample and recording the sensor responses after each addition, the equation becomes

$$Q = (\Delta N + N_0) K \tag{21}$$

where Q is the matrix of volume-corrected responses, one row per addition ($n \times p$), ΔN is the matrix of amounts added at each step ($n \times r$), N_0 is the matrix of initial amounts of each analyte (all rows identical ($n \times r$)), and K is the linear response constants relating each sensor to each analyte ($r \times p$).

Subtracting the initial response for each sensor from all corresponding column elements in Q , a change in response matrix, ΔQ , results with

$$\Delta Q = \Delta N K \tag{22}$$

Because ΔQ and ΔN are known, K can be found using the generalized inverse method. The sensitivity coefficients matrix K is given by

$$K = (\Delta N^T \Delta N)^{-1} \Delta N^T \Delta Q \tag{23}$$

which corrects the analysis for interference and matrix effects.

After estimating K , the vector of initial quantities n_0 can be obtained using the vector of volume-corrected initial responses q_0 by solving

$$q_0 = K^T n_0 \tag{24}$$

The vector n_0 is given by

$$n_0 = (K K^T)^{-1} K q_0 \tag{25}$$

Other chemometrics methods to improve calibration have been advanced. The method of partial least squares has been useful in multicomponent calibration (48–51). In this approach the concentrations are related to latent variables in the block of observed instrument responses. Thus PLS regression can solve the colinearity problem and provide all of the advantages discussed earlier. Principal components analysis coupled with multiple regression, often called Principal Component Regression (PCR), is another calibration approach that has been compared and contrasted to PLS (52–54). Calibration problems can also be approached using the Kalman filter as discussed (43).

Signal Processing and Resolution

Signal processing pertains to a wide collection of tools used to refine the information contained in a raw analytical signal and to estimate pertinent signal parameters such as peak shape, area, and amplitude. Signal processing applications typically involve either energy-variant or time-variant spectra. Techniques such as smoothing and noise filtering are commonly applied to energy or wavelength spectra, whereas time-variant spectra are often processed using methods such as Fourier transforms, Hadamand transforms, and filtering techniques. Peak detection, second or higher derivative spectroscopy, and methods to enhance the signal-to-noise ratio are common applications in signal processing. Image analysis is a particular type of signal processing applied to spatial images in two or more dimensions. An image consists of spectral data obtained as a function of two or more variables, eg, coordinate axes. Methods have been developed to improve the signal-to-noise ratio and sharpen edges within the image. Image restoration methods can reduce blurring and enhance spatial resolution. The field of signal processing methods for chemical signals is an outgrowth of the linear systems theory developed for other digital signals, covered extensively in the electrical engineering literature.

Resolution refers to separating or distinguishing the components of a system and its meaning depends on the nature of the system measurement. In the context of spectroscopy, resolution refers to distinguishing intensities at adjacent wavelengths; in chromatography, resolution is a measure of the separation of chromatographic peaks; in chemical analysis in general, resolution can refer to the estimation of the contributions of components of a mixture to the total analytical response of the sample.

Methods to enhance resolution can be considered in two groups: methods in which assumptions about the system, eg, line shapes, number and or identity of constituent components, are made, and those in which there are no *a priori* assumptions except linear behavior, for instance. An example of the former case is least-squares curve fitting when the spectra of the pure components are known. Another example is in chromatography (qv) when two compounds eluting from the column appear as two overlapping curves. Gaussian peak shape can be assumed and then a sum of two Gaussian functions fit to the overlapping peak. The exact retention times can then be determined and each peak area can be separately integrated.

A method of resolution that makes a very few *a priori* assumptions is based on principal components analysis. The various forms of this approach are based on the self-modeling curve resolution developed in 1971 (55). The method requires a data matrix comprised of spectroscopic scans obtained from a two-component system in which the concentrations of the components are varying over the sample set. Such a data matrix could be obtained, for example, from a chromatographic analysis where spectroscopic scans are obtained at several points in time as an overlapped peak elutes from the column.

Principal component analysis of the data matrix yields eigenvectors, and the proper linear combination of these eigenvectors gives the pure spectra of the individual components contributing to the overlapped peak. By imposing the mathematical constraints that spectra and concentrations must be nonnegative and spectra normalized in area to unity, a range of solutions for the pure spectra can be determined. The band of solutions can be narrowed if there exists at least one unique wavelength, ie, a wavelength where one component absorbs and the other does not. The number of unresolved components under a gas chromatographic peak was determined and estimates calculated of the parent mass spectra (56). This approach has been extended to other hyphenated analytical techniques, such as liquid chromatography–uv-vis spectrophotometry (57) and to three-component matrices (58) (see ANALYTICAL METHODS, HYPHENATED INSTRUMENTS).

Principal component analysis has been used in combination with spectroscopy in other types of multicomponent analyses. For example, compatible and incompatible blends of polyphenylene oxides and polystyrene were distinguished using Fourier-transform-infrared spectra (59). Raman spectra of sulfuric acid–water mixtures were used in conjunction with principal component analysis to identify different ions, compositions, and hydrates (60). The identity and number of species present in binary and tertiary mixtures of polycyclic aromatic hydrocarbons were determined using fluorescence spectra (61).

Kalman filtering has also been used for multicomponent curve resolution. Overlapping curves can be iteratively resolved using mathematical or empirical models. Kalman filters can also be used for real-time resolution of signals in changing conditions, because the method is recursive (42,62). Other strategies are available for resolution of overlapping signals, as well as for signal detection and enhancement (14).

Optimization

Optimization refers to the step in the analytical process (Fig. 2) where some sort of treatment is performed on samples to generate raw data which can be in the form of voltages, currents, or other analytical signals. These data have yet to be calibrated in terms of chemical concentrations.

In the context of chemometrics, optimization refers to the use of estimated parameters to control and optimize the outcome of experiments. Given a model that relates input variables to the output of a system, it is possible to find the set of inputs that optimizes the output. The system to be optimized may pertain to any type of analytical process, such as increasing resolution in hplc separations, increasing sensitivity in atomic emission spectrometry by controlling fuel and oxidant flow rates (14), or even in industrial processes, to optimize yield of a reaction as a function of input variables, temperature, pressure, and reactant concentration. The outputs are the dependent variables, usually quantities such as instrument response, yield of a reaction, and resolution, and the input, or independent, variables are typically quantities like instrument settings, reaction conditions, or experimental media.

The relationship between output variables, called the response, and the input variables is called the response function and is associated with a response surface. When the precise mathematical model of the response surface is not known, it is still possible to use sequential procedures to optimize the system. One of the most popular algorithms for this purpose is the simplex method and its many variations (63,64).

The concept of the simplex algorithm is based on a simple, geometric approach. A simplex is a geometrical figure in n -dimensional space with $n + 1$ vertices. Each vertex represents a set of input variables and their associated response and can be manipulated as a vector in n -space. To begin, three such vectors are selected either at random or by guessing three vectors near the optimal response. Then the vertex that corresponds to the worst response is discarded and is replaced by its reflection. That is, the strategy is to move away from the worst response toward better responses along the direction of the perpendicular bisector of the line between the retained vertices. This process is repeated, as in Figure 16, until it converges to a maximum. If the three initial vertices are A, B, and C, and the point with the worst response is A, then A is replaced by D. In the triangle BCD, if vertex C is found to be the worst, then C is replaced by E, and so forth, until point G is reached and there is no additional improvement. A vertex is replaced by its reflection using the following scheme: let $V_1, V_2, \dots, V_k$ be the vertices of the simplex and let V_i be the vertex which should be eliminated; step 1 is to calculate for $P = 1/(k-1) \sum_{j \neq i} V_j$, and then step 2 is to replace V_i by $V'_i = 2P - V_i$.

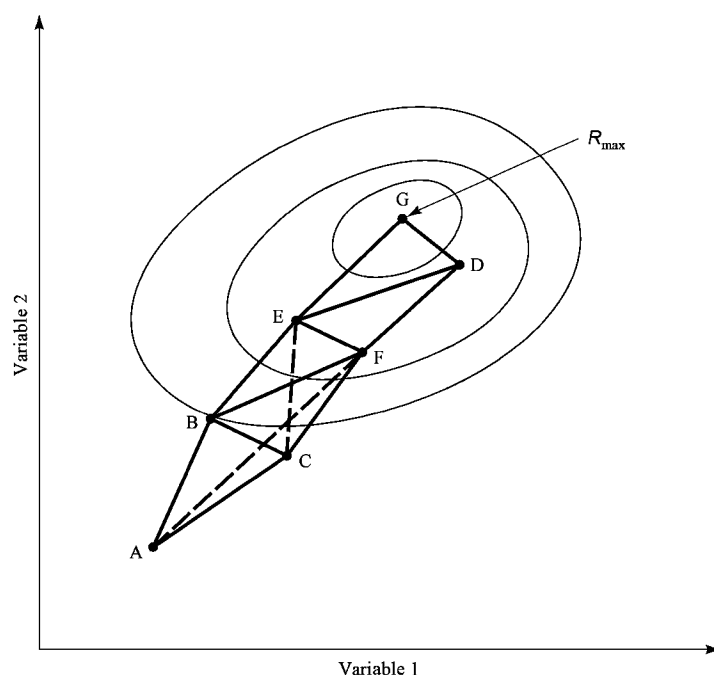


Fig. 16. Schematic diagram of the simple simplex method (14). Reprinted with permission.

The simple simplex method can be modified to accelerate or decelerate movement on the response surface to speed the convergence process. A host of applications of simplex and other optimization methods can be found in the literature. Another aspect of optimization deals with the selection of the optimal number of variables, or the set that maximizes information output or experimental efficiency. For example, a method was developed using principal components analysis to select an optimal subset of sensors (qv) from a larger possible set to detect any given set of analytes (65). Applications of standard experimental design methods such as factorial designs and fractional factorial designs, along with sampling theory, have been reviewed in the chemometrics literature (40–45).

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CHEMOTHERAPEUTICS, ANTHELMINTIC.

See ANTIPARASITIC AGENTS, ANTHELMINTICS; ANTIPARASITIC AGENTS, AVERMECTINS.

CHEMOTHERAPEUTICS, ANTICANCER

Cancer is second only to cardiovascular disease as the principal cause of human mortality (see [CARDIOVASCULAR AGENTS](#)). As the median age of populations have risen, total deaths from cancer have increased. Treatment of cancer includes surgery, radiation, and chemotherapy. In those instances where a tumor is locally confined, has not metastasized, and is resectable, surgery alone or combined with local radiation may be curative. For the majority of patients, however, physicians are forced to rely on chemotherapy either as a means to attack residual disease following surgery and or radiation, or as the primary treatment method. Chemotherapy encompasses the use of both cytotoxic agents and relatively nontoxic hormonal agents for the control of tumor growth (1).

Approaches to cytotoxic chemotherapy include special emphasis on drug targeting and toxicity alleviation. The directions in which new drug discovery strategies are moving and the criteria used for advancing compounds into clinical trials (2) are discussed herein, as are all of the drugs approved by the United States Food and Drug Administration (FDA) for the treatment of cancer as of this writing and those compounds in clinical trials.

Chemotherapeutic Agents

The majority of cytotoxic chemotherapeutic agents in clinical use were discovered empirically using cell cytotoxicity assays followed by assessment in an animal tumor model, usually an *in vivo* leukemia model such as L1210 or P388 (3). On the basis of the activity in those models and other murine solid tumor models, a large number of compounds advanced to human clinical trials where a low percentage were found to have sufficient activity in humans to justify approval as cancer chemotherapeutic agents. It is increasingly clear that these selection criteria were flawed (4). Concurrently, an increased knowledge of the biological complexity of cancer and the mechanism of action of drugs has permitted the design of more rational screens for the discovery of new lead structures and the design and synthesis of compounds targeted to specific receptors or enzymes involved in the pathogenesis of cancer (5).

At the preclinical level of discovery in the 1990s there is a greater reliance on the use of human tumor cell lines and clonogenic assays derived from primary explants (6). As the development of resistance to cytotoxic agents by tumor cells is better understood, it has become possible to assemble panels of cell lines consisting of a parent cell line and one or more resistant cell lines wherein the mechanism of resistance has been identified and quantitated, ie, expression of multidrug resistant (MDR) genes, increased glutathione [70-18-8]/levels, and increased DNA repair. The use of mechanism-based screens such as specific oncogene tyrosine kinase assays, topoisomerase I and or II assays, and tubulin assays has also become possible (5).

At the *in vivo* assay level, the classic ip-ip (interaperitoneal) *in vivo* model has been replaced as a selection criteria for advancement of new drug candidates to clinical trial. More stringent alternative models include subcutaneous or subrenal capsule implantation of tumor followed by intravenous drug dosing (7) and the human tumor xenograft models in nude mice (8).

In addition to a greater emphasis on *in vivo* evaluation as a means of assessing activity, there is also increased awareness of metabolism and pharmacokinetics in candidate selection (9). The use of prodrug strategies to improve water solubility, oral absorption, and other pharmaceutical properties has increased (10). Finally, the ability to assess potential toxic liabilities of a new drug candidate has improved as more predictive models for myelosuppression, ie, neutropenia and thrombocytopenia, emesis, and renal, cardiac, and hepatic toxicities, have been developed (11,12).

The modern drug discovery team consists of medicinal chemists, biologists, metabolism and pharmacokinetics specialists, and toxicologists working together to improve drug selection.

Drugs used in cancer chemotherapy or clinical trials are classified according to primary underlying mechanisms of action. However, many drugs operate through multiple mechanisms. Mechanisms include those of antimetabolites, DNA alkylating and or cross-linking agents, DNA binding cleaving agents, DNA topoisomerase interactive compounds, agents which act on tubulin structure, and hormones (qv) (Fig. 1). In addition to those drugs which have already been approved by the FDA, a number of investigational drugs are undergoing clinical evaluation and many others are in the pipeline.

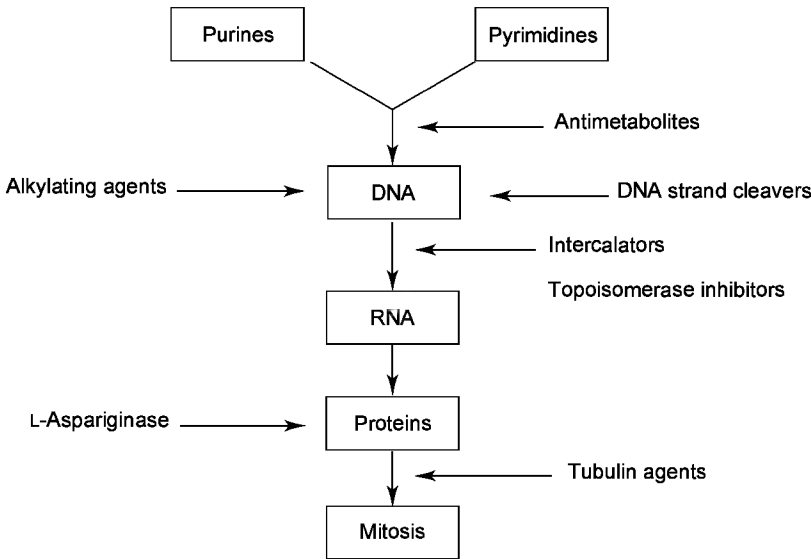


Fig. 1. Schematic of nucleic acid and protein synthesis and the steps leading to mitosis showing the common mechanisms of action and various classes of chemotherapeutic agents.

Antimetabolites. Antimetabolites, which represent one of the earliest groups of anticancer agents, are listed in Table 1. Structures are shown in Fig. 2.

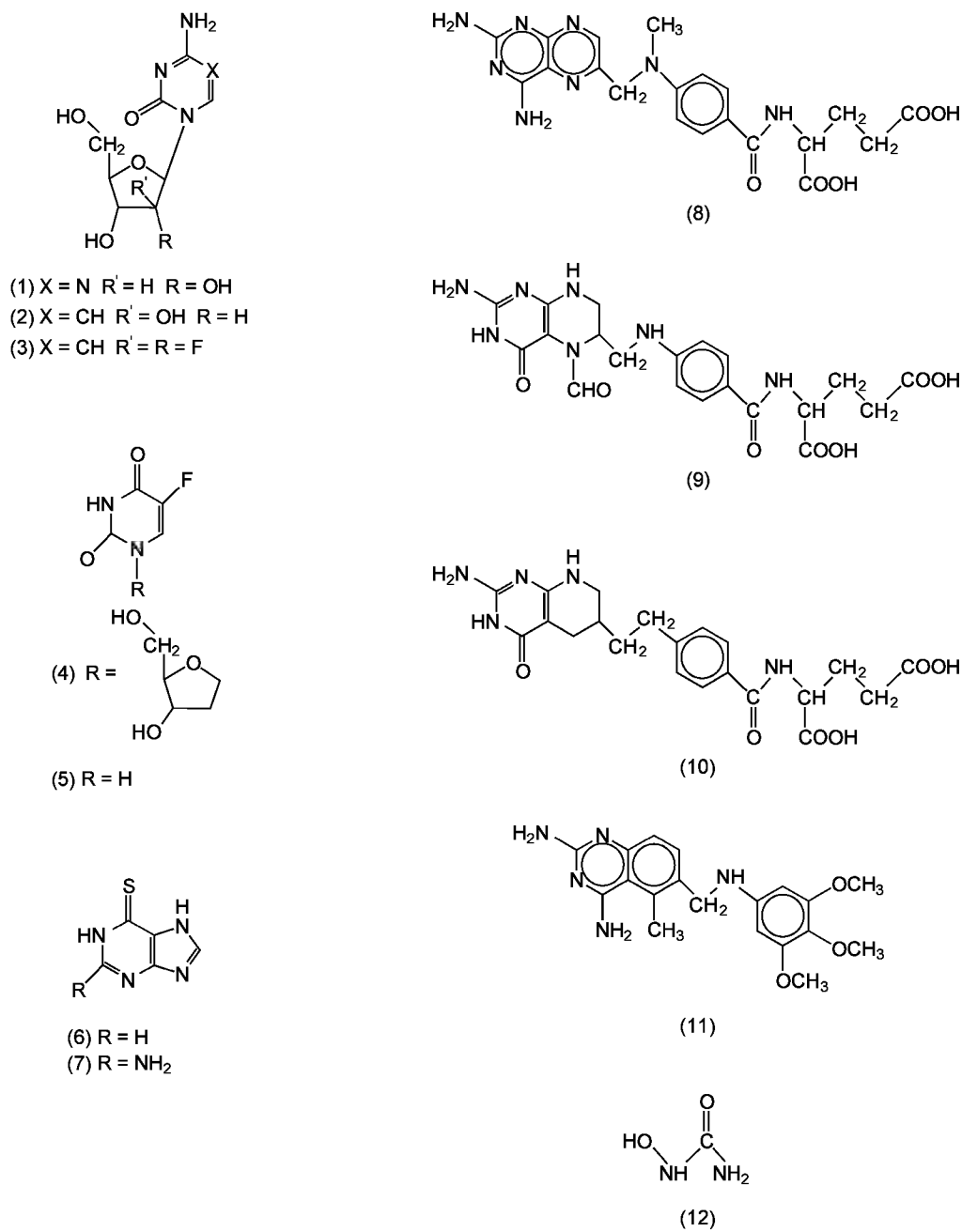


Fig. 2. Structures of antimetabolites listed in Table 1.

Table 1. Antimetabolites^a

Drug (trade name)	CAS Registry Number	Molecular formula	Molecular weight	Structure number	Disease	Toxic effects
5-azacitidine ^b (Mylosar)	[320-67-2]	C ₈ H ₁₂ N ₄ O ₅	244.21	(1)	acute myelogenous leukemia	nausea, vomiting; hepatic dysfunction; myelosuppression
cytarabine USP ^b (Cytosar)	[147-94-4]	C ₉ H ₁₃ N ₃ O ₅	243.22	(2)	acute granulocytic leukemia (adults); acute lymphocytic leukemia (children); Hodgkin's disease	bone-marrow depression; hepatic toxicity; megaloblastosis; nausea; vomiting; diarrhea
gemcitabine ^c	[95058-81-4]	C ₉ H ₁₁ F ₂ N ₃ O ₄	263.20	(3)	investigational drug; responses seen in Phase I trials in colon and nonsmall cell lung cancer	myelosuppression observed as dose limiting toxicity
floxuridine USP ^d (FUDR)	[50-91-9]	C ₉ H ₁₁ FN ₂ O ₅	246.21	(4)	palliative treatment of gastrointestinal adenocarcinoma with liver metastases	severe hematological toxicity; gastrointestinal hemorrhage; nausea; vomiting; diarrhea; enteritis; stomatitis; erythema
fluorouracil USP ^d (Fluorouracil)	[51-21-8]	C ₄ H ₃ FN ₂ O ₂	130.08	(5)	palliative treatment of carcinoma of colon, rectum, breast, stomach, and pancreas	bone-marrow depression; dermatitis; alopecia; nausea; vomiting; diarrhea; stomatitis; anorexia; GI ulcers; skin

mercaptopurine USP ^e (Purinethol)	[6112-76-1]	C ₅ H ₄ N ₄ S	152.19	(6)	acute leukemia (more effective in children than in adults); chronic granulocytic leukemia	pig-mentation bone-marrow depres-sion; hepatic toxic-ity; anemia; gas-trointestinal (GI) ulceration; nausea; vomiting
thioguanine USP ^e (Tabloid)	[154-42-7]	C ₅ H ₅ N ₅ S·XH ₂ O	167.19	(7)	acute leukemia; chronic granulocytic leukemia	bone-marrow depres-sion; stomatitis; an-orexia; nausea; vom-iting
methotrexate ^f USP (Methotrexate)	[59-05-2]	C ₂₀ H ₂₂ N ₈ O ₅	454.46	(8)	acute lymphocytic leu-kemia; meningeal leukemia; choriocar-cinoma; choriaden-oma destruens; lym-phosarcoma; osteogenic sarcoma; cancer of lung, neck, head, cervix; my-cosis fungoides; hy-datidiform mole high dose MTX fol-lowed by leucovorin rescue in nonmetas-tatic osteosarcoma	bone-marrow depres-sion; renal and he-patic toxicity; enteri-tis; stomatitis; alo-pecia; abdominal dis-tress; erythematous rash; oral and GI ul-ceration; diarrhea; nausea; vomiting
leucovorin ^f (calcium USP)	[58-05-9]	C ₂₀ H ₂₁ CaN ₇ O ₇	511.51	(9)	high dose methotrex-ate rescue therapy in osteosarcoma	allergic sensitization
DDATHF ^c (Ly237147) (Lome-trexol sodium)	[120408-07-3]	C ₂₁ H ₂₃ N ₅ Na ₂ O	487.42	(10)	investigational drug	
trimetexate ^g	[52128-35-5]	C ₁₀ H ₂₃ N ₅ O ₃	369.42	(11)	investigational drug; partial remissions in soft tissue sarcomas observed	myelosuppression; mu-cositis; nausea; vom-iting; skin rash
hydroxyurea USP ^h (Hydrea)	[127-07-1]	CH ₄ N ₂ O ₂	76.05	(12)	chronic granulocytic leukemia; mela-noma; cancer of ovary, head, neck	vomiting; anorexia; fe-ver; bone-marrow depression; nausea; diarrhea

^a See Figure 2.
^b Upjohn.
^c Lilly.
^d Hoffmann-La Roche.
^e Burroughs Wellcome.
^f Lederle.
^g Parke-Davis.
^h Bristol-Myers Squibb

The classification of these drugs as antimetabolites stems from the mode of action as antagonists to the natural metabolic processes leading to either DNA, RNA, or protein synthesis (13) (see NUCLEIC ACIDS; PROTEINS). They either inhibit function of a key enzyme involved in protein synthesis or are recruited into the cell division process as DNA synthesis terminators. For example, methotrexate (8) is a folic acid [59-30-3], C₁₀H₁₀N₇O , antagonist and has a 100,000-fold greater affinity for the enzyme, dihydrofolate reductase [9002-03-3] (DHFR), than does the enzyme's natural substrate, folic acid. Inhibition of DHFR function, ie, conversion of folic acid to folinic acid [58-05-9] (leucovorin) (9), results in the arrest of purine and pyrimidine synthesis which culminates in cell death. The use of high dose methotrexate treatment followed by leucovorin rescue, ie, toxicity amelioration, has resulted in significant improvements in the treatment of nonmetastatic osteosarcoma. In the early 1990s, the use of high dose regimens followed by rescue with colony stimulating factors (CSFs) (14) has been extended to bone marrow transplantation.

Antimetabolites may be further classified as inhibitors of pyrimidine, purine, or glutamine metabolism. The compounds are cell cycle dependent.

DNA Alkylating/Cross-Linking Agents. This category includes compounds of diverse chemical classes (Table 2) eg, nitrosoureas (13–16) nitrogen mustards (18–24), mitomycins (25–27), and platinum (28,29), that have the ability to react covalently with DNA bases and to form inter- and intrastrand DNA cross-links (15–17). These compounds may also be responsible for the alkylation of proteins and protein–DNA linkages. The resulting lesions produced in the DNA result in disruption of cell growth and function, ultimately leading to cell death. The onset of action of this class of agents can be rapid, resulting in dramatic tumor shrinkage. However, because of the effects on normal cells, all compounds of this class are myelosuppressive and potentially teratogenic, mutagenic, and carcinogenic. In some cases the resulting myelosuppression has limited the ability of these drugs to be effective clinically. In other cases the rapid onset of resistance can occur; this limits utility as well as that of related analogues, because of cross resistance (18) (Fig. 3).

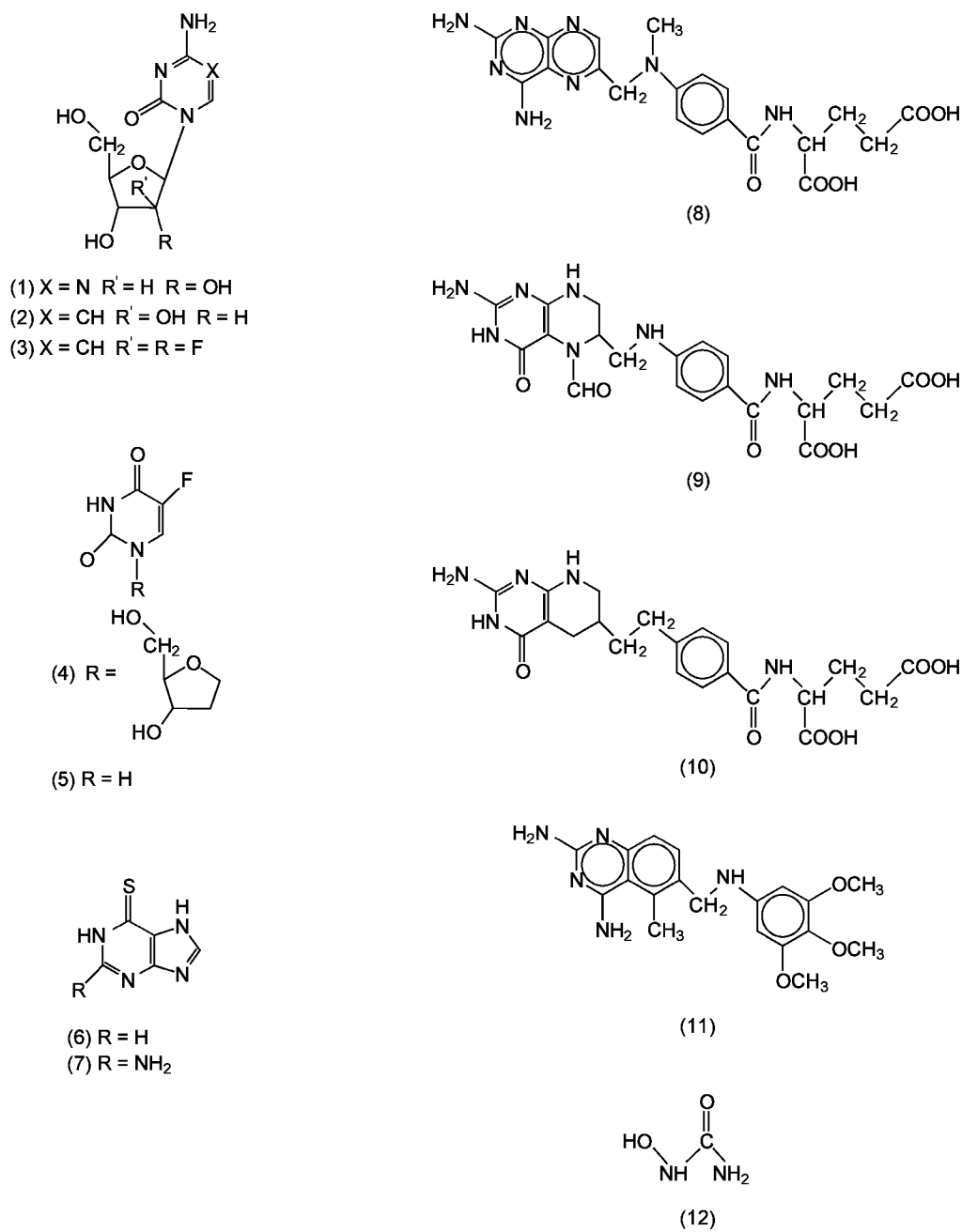


Fig. 3. Structures of DNA alkylating cross-linking agents given in Table 2.

Table 2. DNA Alkylating/Cross-Linking Agents^a

Drug (trade name)	CAS Registry Number	Molecular formula	Molecular weight	Structure number	Disease	Toxic effects
carmustine USP ^b (BiCNU)	[154-93-8]	C ₅ H ₉ Cl ₂ N ₃ O ₂	214.05	(13)	Hodgkin's disease; non-Hodgkin's lym-phomas; meningeal leukemia; brain tu-mor; multiple mye-loma	bone-marrow depres-sion; hepatic toxic-ity; nausea; vomit-ing
lomustine USP ^b (CeeNU)	[13010-47-4]	C ₉ H ₁₁ ClN ₃ O ₂	233.70	(14)	malignant brain tu-mors; Hodgkin's dis-ease	bone-marrow depres-sion; hepatic toxicity
taumustine ^c	[85977-49-7]	C ₇ H ₁₅ ClN ₄ O ₄ S	286.73	(15)	investigational drug responses observed in malignant mela-noma	gastrointestinal; thrombocytopenia
streptozocin USP ^d (Zanosar)	[18883-66-4]	C ₈ H ₁₅ N ₃ O ₇	265.22	(16)	metastatic islet cell carcinoma of the pancreas	bone-marrow depres-sion; renal and he-patic toxicity; nau-sea; vomit-ing
busulfan USP ^e (Myleran)	[55-98-1]	C H ₁₄ O S ₂	246.29	(17)	chronic granulocytic leukemia; other myeloproliferative disorders	bone-marrow depres-sion; hyperuricemia; gynecomastia; amenorrhea; skin hyperpigmentation
cyclophosphamide USP ^b (Cytoxan)	[6055-19-2]	C ₇ H ₁₅ Cl ₂ N ₂ O ₂ P	279.10	(18)	acute and chronic lym-phocytic leukemia; lung cancer; rhab-domyosarcoma; neuroblastoma; ovarian and mam-mary	bone-marrow depres-sion; hepatic toxic-ity; cystitis; alope-cia; nausea; vomiting

					carcinoma; multiple myeloma; lymphosarcoma; Burkitt's lymphoma; Hodgkin's disease; retinoblastoma; my-cosis fungoides	
ifosphamide USP ^b (Ifex)	[3778-73-2]	C ₇ H ₁₅ Cl ₂ N ₂ O ₂ P	261.09	(19)	germ cell testicular cancer; used in com-bination with mesna	myelosuppression; urotoxicity; alopecia; nausea; vomiting; CNS toxicities
mesna USP ^b (Mesnex)	[19767-45-4]	C ₂ H ₅ NaO ₃ S ₂	164.17	(20)	prophylactic preven-tion of hemorrhagic cystitis	
mechlorethamine hydrochloride USP ^f (Must-argen)	[55-86-7]	C ₅ H ₁₁ Cl ₂ N · HCl	192.52	(21)	Hodgkin's disease; non-Hodgkin's lym-phomas; lymphosar-coma; cancer of breast, ovary, lung; neoplastic effusion	bone-marrow depres-sion; nausea; vomit-ing; anorexia; diar-rhea; local irritation
chlorambucil USP ^e (Leukeran)	[305-03-3]	C ₁₄ H ₁₉ Cl ₂ NO ₂	304.22	(22)	chronic lymphocytic leukemia; cancer of ovary, breast, testis; Hodgkin's disease; non-Hodgkin's lym-phomas	bone-marrow depres-sion; nausea; vomit-ing
melphalan USP ^e (Alkeran)	[148-82-3]	C ₁₃ H ₁₈ Cl ₂ N ₂ O ₂	305.20	(23)	multiple myeloma; plasmacytic mye-loma; cancer of breast and ovary	bone-marrow depres-sion; nausea; vomit-ing; anorexia
thiotepa USP ^g (Thiotepa)	[52-24-4]	C H ₁₂ N ₃ PS	189.21	(24)	cancer of breast, ovary, lung, bladder; Hodgkin's disease; nonHodgkin's lym-phomas; neoplastic effusion	bone-marrow depres-sion; amenorrhea; anorexia; nausea; vomiting
mitomycin C USP ^b (Muta-mycin)	[50-07-7]	C ₁₅ H ₁₈ N ₄ O ₅	334.33	(25)	chronic myelogenous leukemia; reticulum cell sarcoma; Hodg-kin's disease; non-Hodgkin's lympho-mas; cancer of stomach, pancreas, lung; epithelial tu-mors	bone-marrow depres-sion; renal toxicity; alopecia; stomatitis; anorexia; nausea; vomiting
BMY-2506 ^{7b}	[95056-36-3]	C ₂₃ H ₂₅ N ₅ O ₇ S ₂	547.60	(26)	investigational drug	
KW2149 ^h	[118359-59-4]	C ₂₄ H ₃₄ N O ₈ S ₂	598.70	(27)	investigational drug	
cisplatin USP ^b (Platinol)	[15663-27-1]	Cl ₂ H N ₂ Pt	300.06	(28)	metastatic testicular tumors; metastatic ovarian tumors; ad-vanced bladder can-cer	nephrotoxicity; ototox-icity; myelosuppres-sion; nausea; vomit-ing; allergic reaction
carboplatin USP ^b (Paraplatin)	[41575-94-4]	C H ₁₂ N ₂ O ₄ Pt	371.25	(29)	recurrent ovarian carcinoma	bone-marrow suppres-sion; emesis; allergic reactions
dacarbazine USP ⁱ (DTIC)	[4342-03-4]	C H ₁₀ N O	182.18	(30)	malignant melanoma; Hodgkin's disease; soft tissue sarcomas	bone-marrow depres-sion; flulike syn-drome; alopecia; nausea; vomiting; anorexia

^a See Figure 3.
^b Bristol-Myers Squibb.
^c Pharmacia.
^d Upjohn.
^e Burroughs Wellcome.
^f Merck Sharp & Dohme.
^g Lederle.
^h Kyowa-Hakko.
ⁱ Dome.

DNA Binding/Cleaving Agents. DNA binding and or cleaving agents that have anticancer activity are listed in Table 3. Structures are shown in Fig. 4. All of the natural products (31,32,35,36,38,39) and analogues of natural products (33,34,37) in this category (Table 3) are able to bind DNA either as intercalators (31–34) or as minor groove binders (35–37), hence inhibiting DNA dependant RNA synthesis (15–17). Both bleomycin (35) and esperamicin A₁ (36) cleave DNA by forming free radicals in the immediate vicinity of the sugar–phosphate backbone. Activity as antitumor agents is related to the ability to induce irreparable lesions in DNA (15,19). Bleomycin generates oxygen free-radical species whereas esperamicin A₁ and a number of related natural products that include neocarzinostatin, dynemicin, and the calicheamicins, generate aryl diradical species, which abstract hydrogen atoms directly from the deoxyribose backbone (19). An analogue of the natural product CC1065 (37) has the unique property of being a DNA alkylating agent which recognizes poly-AT regions of the minor groove of DNA. It remains to be seen if the high potency and unique modes of action ascribed to these novel classes of agents can translate into clinically useful drugs (Figure 4) (20).

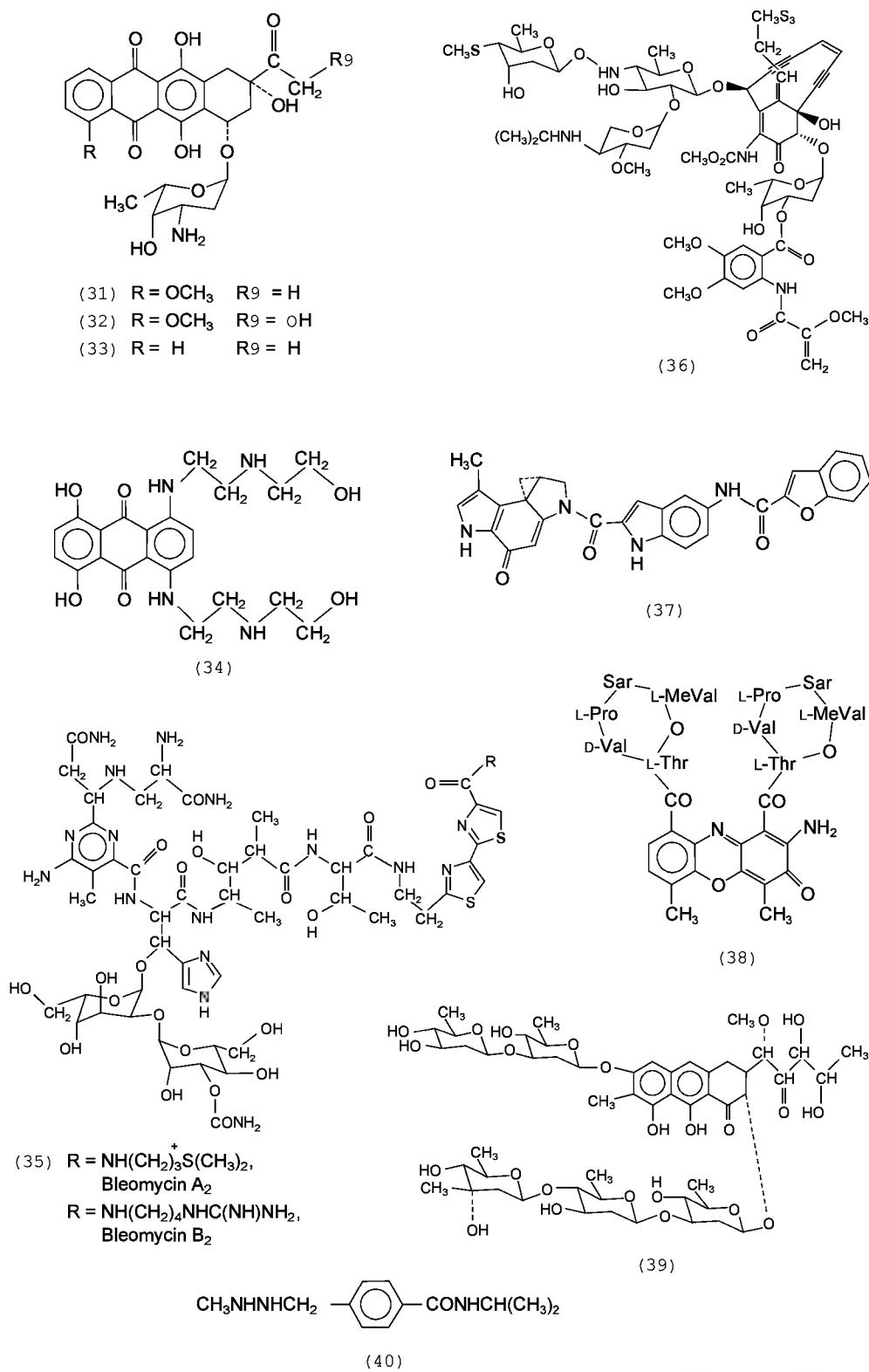


Fig. 4. Structures of DNA interactive agents are given in Table 3. In structure (38) L-MeVal is 1-N-methyl valine.

Table 3. DNA Interactive Agents^a

Drug (trade name)	CAS Registry Number	Molecular formula	Molecular weight	Structure number	Disease	Toxic effects
daunorubicin hydrochloride USP ^b (Cerubidine)	[20830-81-3]	C ₂₇ H ₂₉ NO ₁₀ ·HCl	563.99	(31)	acute lymphocytic and granulocytic leuke-mia; lymphomas	bone-marrow depres-sion; cardiac toxic-ity; alopecia; stoma-titis; GI disturbance
doxorubicin USP ^c (Adriamycin)	[23214-92-8]	C ₂₇ H ₂₉ NO ₁₁	543.53	(32)	soft-tissue and osteo-genic sarcomas; Hodgkin's disease; non-Hodgkin's lym-phomas; acute leuke-mia; cancer of thy-roid, breast, lung, genitourinary (GU) tract; Wilm's tumor; neuroblastoma	bone-marrow depres-sion; cardiac toxic-ity; alopecia; stoma-titis; GI disturbance
idarubicin	[57852-57-0]	C ₂ H ₂₇ NO ₉ ·HCl	533.96	(33)	acute myeloid leuke-mia in	bone-marrow

hydrochloride ^c (Idamycin)					adults	suppres-sion; cardiotoxicity; nausea; vomiting; alopecia
mitoxanthrone hydrochloride USP ^d (Novantrone)	[70476-82-3]	C ₂₂ H ₂₈ N ₄ O ·2H Cl	517.41	(34)	acute nonlymphocytic leukemia including myelogenous pro-myelocytic, monocy-tic and erythroid acute leukemias	nausea; vomiting; alo-pecia; mucositis; sto-matitus; myelo-suppression; cardio-toxicity; allergic reaction; phlebitis
bleomycin sulfate USP ^e (Blenoxane)	[11056-06-7]	mixture of bleo-mycin A ₂ , B ₂ as primary components		(35)	squamous cell carci-noma of head, neck, esophagus, skin, GU tract; testicular tu-mor; Hodgkin's lym-phomas	pulmonary fibrosis; skin reactions; alo-pecia; nausea; vom-iting; anorexia; fe-ver; stomatitis
esperamicin A ₁ ^e	[99674-26-7]	C ₅₀ H ₈₀ N ₄ O ₂₂ S ₄	1324.41	(36)	investigational drug	
Adozelesin ^f (U73,975)	[110314-48-2]	C ₃₀ H ₂₂ N ₄ O ₄	502.30	(37)	investigational drug	
dactinomycin USP ^g (Cosmegen)	[50-76-0]	C ₂ H ₈ N ₁₂ O ₁	1255.43	(38)	Wilm's tumor; Ewing's tumor; choriocarci-noma; testicular car-cinoma; rhabdo-myosarcoma; neuroblastoma; melanoma; soft-tissue and osteo-genic sarcomas	bone-marrow depres-sion; renal and hepatic toxicity; alo-pecia; mental depression; stomati-tis; nausea; vomit-ing; diarrhea; an-orexia; local irritation
plicamycin USP ^h (Mithracin)	[18378-89-7]	C ₅₂ H ₇ O ₂₄	1085.16	(39)	testicular tumors; hy-percalcemia and hy-percalciuria associ-ated with advanced malignancies	bone-marrow depres-sion; hepatic and renal toxicity; hypo-calcemia; hemor-rhage; stomatitis; nausea; vomiting; anorexia; diarrhea
procarbazine hydrochloride USP ⁱ (Matulane)	[366-70-1]	C ₁₂ H ₁₉ N ₃ O ·HCl	257.76	(40)	Hodgkin's disease; non-Hodgkin's lym-phomas; lung cancer	bone-marrow depres-sion; neurological and dermatological toxicity; nausea; vomiting

^a See Figure 4.
^b Wyeth-Ayerst.
^c Adria.
^d Lederle.
^e Bristol-Myers Squibb.
^f UpJohn.
^g Merck Sharp & Dohme.
^h Miles.
ⁱ Hoffmann-La Roche.

Topoisomerase Interactive Drugs. Topoisomerases I and II have emerged as interesting targets for the design of new anticancer agents (15,21) (Table 4). Etoposide (41) and related epipodophyllotoxin analogues (42,43) produce DNA strand scission via the mediation of topoisomerase II. Additional work with other clinically active agents, such as adriamycin (32) and ansacrine (47), indicate that these compounds interact with topoisomerase also. A number of drugs are known to work on topoisomerase II only. However, camptothecin [7689-03-4] and its analogues, CPT 11 (44) and topotecan (45), have been shown to target topoisomerase I (22). Encouraging solid tumor activity of these agents in Phase I trials has sparked an intense effort to identify further examples of topoisomerase I inhibitors (Fig. 5).

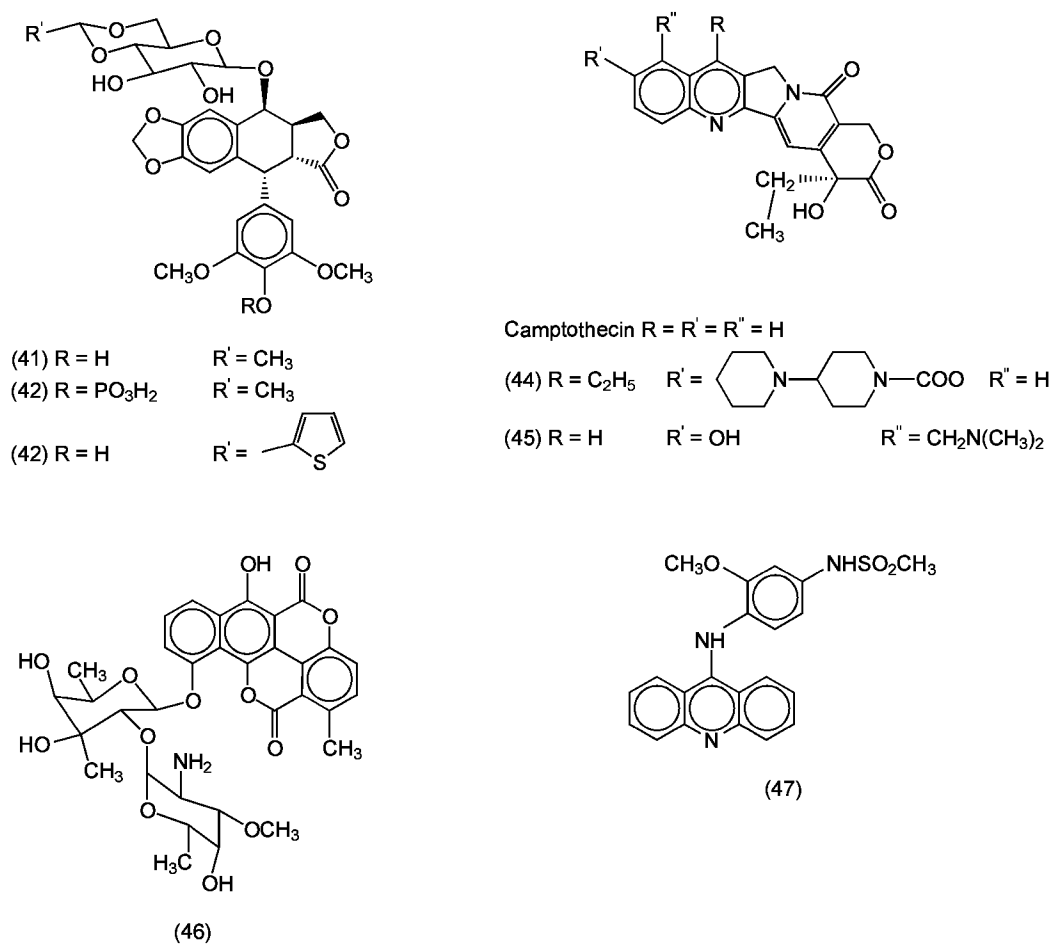


Fig. 5. Structures of topoisomerase interactive drugs given in Table 4.

Table 4. Topoisomerase Interactive Drugs^a

Drug (trade name)	CAS Registry Number	Molecular formula	Molecular weight	Structure number	Disease	Toxic effects
etoposide USP ^b (Vepesid)	[33419-42-0]	C ₂₉ H ₃₂ O ₁₃	588.56	(41)	refractory testicular tumors; small cell lung cancer	myelosuppression; mild to moderate nausea and vomit-ing; transient hypo-tension; allergic re-actions; alopecia
etoposide	[117091-64-2]	C ₂₉ H ₃₃ O ₁ P	712.51	(42)	investigational drug; prodrug of etoposide	prodrug of etoposide
phosphatetoposide ^b	[29767-20-2]	C ₃₂ H ₃₂ O ₁₃ S	656.67	(43)	refractory acute lym-phocytic leukemia in children	myelosuppression; mild to moderate nausea and vomit-ing; transient hypo-tension; allergic re-actions; alopecia
CPT-11 ^c	[100286-90-6]	C ₃₃ H ₃₈ N ₄ O ·HCl	622.78	(44)	investigational drug; topoisomerase I in-hibitor	
topotecan hydro-chloride ^d	[119413-54-6]	C ₂₃ H ₂₃ N ₃ O ₅ ·HCl	457.91	(45)	investigational drug; topoisomerase I in-hibitor	
elsamitrucin tartrate ^b	[123303-9S-7]	C ₃₃ H ₃₅ NO ₁₃ ·C ₄ H ₄ O ₄	771.37	(46)	investigational drug	
amsacrine ^e (Amsidyl)	[51264-14-3]	C ₂₁ H ₁₉ N ₃ O ₃ S	393.46	(47)	investigational drug	

^a See Figure 5.

^b Bristol-Myers Squibb.

^c Yakult Honsha.

^d Smith Kline Beecham.

^e Parke-Davis.

Tubulin Active Drugs. Vinblastin (48) and vincristin (49), two very useful natural products derived from Vinca rosea (periwinkle plant), were discovered in the early days of cancer chemotherapy (Table 5), (Fig. 6). (23). Vinblastin and vincristin are highly cell cycle dependent. They disrupt the mitotic spindle by promoting the disassembly of the microtubules essential for cell division. This results in cell death during replication. Vinblastin and vincristin differ minimally from one another structurally, but have different clinical utilities. A search for additional members of the Vinca alkaloid family has resulted in two new investigational drugs, vindesine (50) and navelbine (51) (24) (see ALKALOIDS), currently undergoing clinical trial. Initial results using navelbine indicate that this compound may find use in nonsmall cell lung cancer (25).

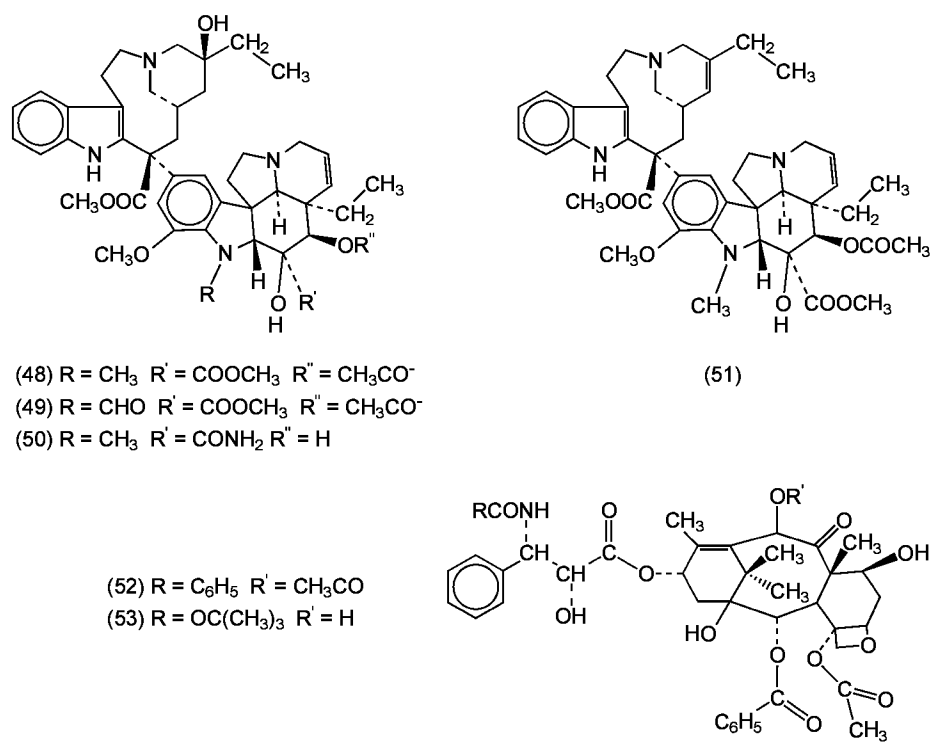


Fig. 6. Structures of tubulin active drugs listed in Table 5.

Table 5. Tubulin Active Drugs^a

Drug (trade name)	CAS Registry Number	Molecular formula	Molecular weight	Structure number	Disease	Toxic effects
vinblastin sulfate USP ^b (Velban)	[143-67-9]	C ₄ H ₅₈ N ₄ O ₉ ·H ₂ SO ₄	909.06	(48)	Hodgkin's disease; lymphosarcoma; re-ticulum-cell sar-coma; neuroblas-toma; choriocarcinoma; carcinoma of breast, lung, oral cavity, testis, bladder; acute and chronic leuke-mia; histiocytosis; mycosis fungoides	leukopenia; neurologi-cal toxicity (pares-thesias, mental depression, loss of deep tendon re-flexes, etc); dysfunc-tion of autonomic nervous system (ileus, constipation, urinary retention, etc); alopecia; sto-matitis; nausea; vomiting; local irri-tation
vincristin sulfate USP ^b (Oncovin)	[2068-78-2]	C ₄ H ₅ N ₄ O ₁₀ ·H ₂ SO ₄	923.04	(49)	acute leukemia in chil-dren; lymphocytic leukemia; Hodgkin's disease; non-Hodg-kin's lymphomas; Wilm's tumor; neuroblastoma; rhabdomyosarcoma.	neurological toxicity (paresthesias, foot drop, double vision, etc); constipation; ileus; alopecia; leu-kopenia (occasional);
vindesine sulfate ^b (Eldisine)	[59917-39-4]	C ₄₃ H ₅₅ N ₅ O ₇ ·H ₂ SO ₄	852.01	(50)	investigational drug	
navelbine ^c (Vinorelbine)	[71486-22-1]	C ₄₅ H ₅₄ N ₄ O ₈	778.45	(51)	investigational drug; nonsmall cell lung cancer	
taxol ^d	[33069-62-4]	C ₄₇ H ₅₁ NO ₁₄	853.92	(52)	investigational drug; refractory ovarian cancer; refractory breast cancer; mela-noma; lung cancer; head and neck can-cer	alopecia; neutropenia; hypersensitivity; mucositis; neuropa-thy
taxotere ^e (Docetaxol)	[114977-28-5]	C ₄₃ H ₅₃ NO ₁₄	807.43	(53)	investigational drug	

^a See Figure 6.
^b Lilly.
^c Pierre Fabre.
^d Bristol-Myers Squibb.
^e Rhône-Poulenc.

Taxol (52), a compound isolated from the pacific yew tree *Taxus brevifolia* (26), has shown high response rates in a variety of solid tumors including refractory ovarian cancer, refractory breast cancer, head and neck cancer, melanoma, and lung cancer. The mechanism of action for taxol is also linked with tubulin. However, unlike the Vinca alkaloids, taxol accelerates tubule formation and stabilizes it to depolymerization (27). The clinical development of taxol is dependent on identifying a renewable source. Once the FDA approves this drug for therapeutic use, large (kilogram) quantities are expected to be needed for the treatment of large patient populations. Approaches being investigated to address the problem of renewable source include cultivation, tissue culture, semisynthesis, and total synthesis (28). Resolution of supply problems also are needed to permit exploration of the full potential of this drug.

In addition to the Vinca alkaloids and taxol, a limited number of other cytotoxic agents have been demonstrated to act at the level of tubulin. This

list includes colchicine [64-86-8] and the various podophyllotoxins and further underscores the importance of tubulin and microtubule formation as targets for anticancer drug action.

Hormones. Although not strictly cytotoxic, hormones (qv) have been used to control the environment of hormone dependent tumors such as those of the prostate, breast, and endometrium (29), ie, androgens are used to control the growth of estrogen dependent breast tumors, whereas estrogens control androgen dependent tumors of the prostate. Hormones that have anticancer activities are listed in Table 6. Structures are shown in Figure 7. In addition to the steroidal hormones (57, 59–62) several nonsteroidal hormones have been introduced (54–56) as have leutenizing hormone-releasing hormone (LHRH) agonists. These are often used in combinations. For example, LHRH analogues (63,64), antiestrogens (54), aromatase inhibitors (62), and progestins all are used in the control of breast cancer (30). LHRH analogues suppress estrogen production in the ovaries and are used in premenopausal breast cancer patients.

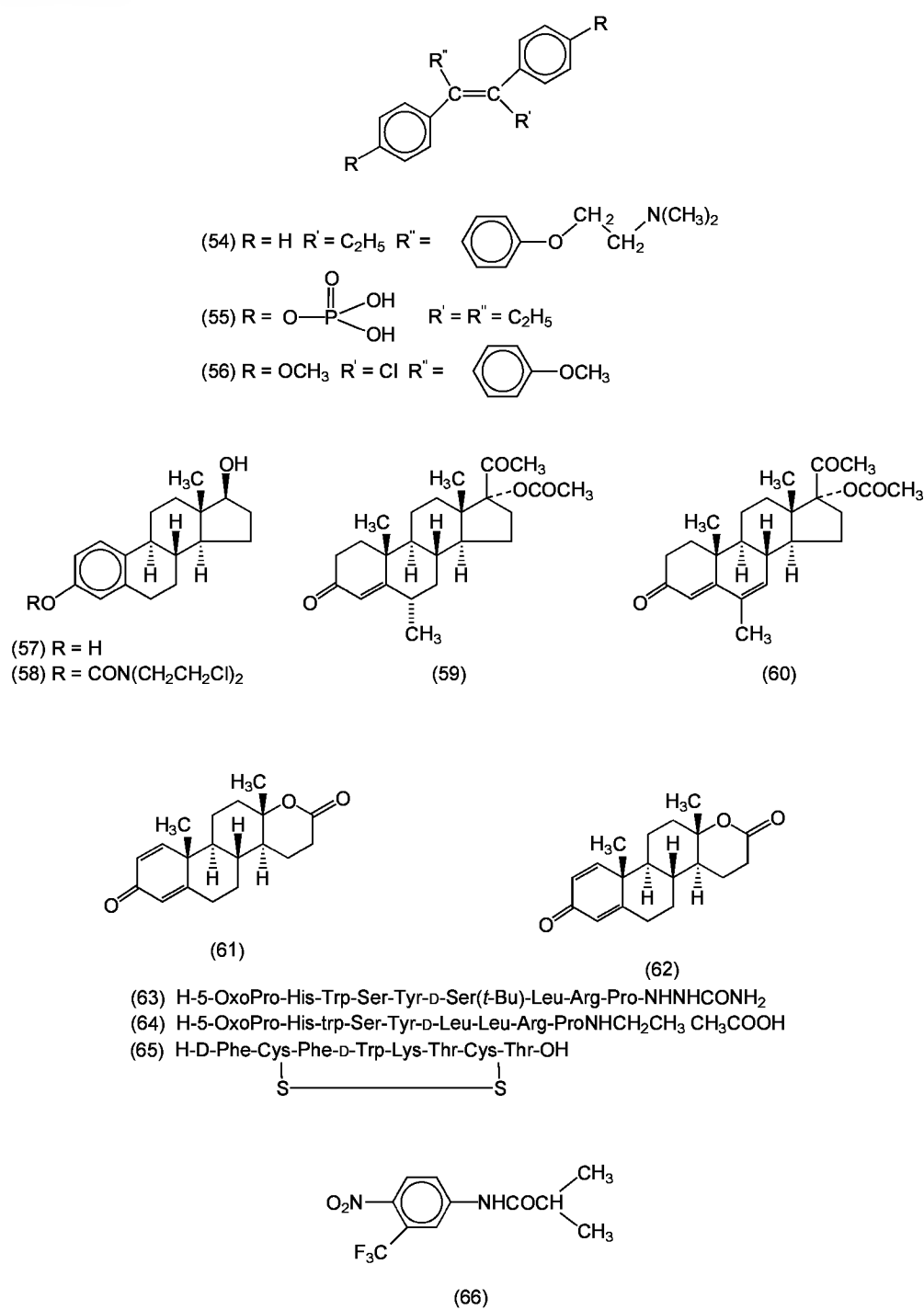


Fig. 7. Structures of hormone chemotherapeutic agents given in Table 6.

Table 6. Hormonal Therapy^a

Drug (trade name)	CAS Registry Number	Molecular formula	Molecular weight	Structure number	Disease	Toxic effects
tamoxifen citrate USP ^b (Nolvadex)	[54965-24-1]	C ₂₂ H ₂₉ NO·C ₆ H ₈ O ₇	563.65	(54)	breast cancer	visual disturbances
diethylstilbestrol diphosphate USP ^c (Stilphos-trol)	[522-40-7]	C ₁₈ H ₂₂ O ₈ P ₂	428.31	(55)	prostatic carcinoma	fluid retention; hyper-calcemia; common side effects of steroids
chlorotrianisene USP ^c (TACE)	[569-57-3]	C ₂₃ H ₂₁ ClO ₃	380.87	(56)	androgen dependent carcinoma of the prostate	fluid retention; hyper-calcemia; common side effects of steroids
estradiol USP ^d (Estrace)	[50-28-2]	C ₁₈ H ₂₄ O ₂	272.39	(57)	breast cancer; pros-tatic carcinoma	fluid retention; hyper-calcemia; common

estramustine phosphate so-dium USP ^e (Emcyt)	[52205-73-9]	C ₂₃ H ₃₀ Cl ₂ N ·Na ₂ O P	564.35	(58)	prostatic carcinoma	side effects of steroids side effects because of estradiol; increased dyspnea; nausea; vomiting
medroxyproges-terone acetate ^f (USP Depo-provera)	[71-58-9]	C ₂₄ H ₃₄ O ₄	386.53	(59)	metastatic endome-trial carcinoma; renal carcinoma	fluid retention; hyper-calcemia; common side effects of steroids
megestrol acetate USP ^d (Megace)	[595-33-5]	C ₂₄ H ₃₂ O ₄	384.51	(60)	carcinoma of the breast or endrome-trium	fluid retention; hyper-calcemia; common side effects of steroids
testolactone USP ^d (Teslac)	[968-93-4]	C ₁₉ H ₂₄ O ₃	300.40	(61)	breast cancer	fluid retention; hyper-calcemia; common side effects of steroids
formestane ^g (Lentaron)	[566-48-3]	C ₁₉ H ₂ O ₃	302.41	(62)	investigational drug; postmenopausal breast cancer	
goserelin USP ^b (Zoladex)	[65807-02-5]	C ₅₉ H ₈₄ N ₁₈ O ₁₄	1269.43	(63)	prostatic carcinoma	bone pain; common hormonal side effects
leuprolide ace-tate USP ^h (Leupron)	[74381-53-6]	C ₅₉ H ₈₄ N ₁ O ₁₂ ·C ₂ H ₄ O ₂	1269.47	(64)	prostatic carcinoma	common hormonal side effects
octreotide ace-tate USP ⁱ (Sandostatin)	[79517-01-4]	C ₄₉ H N ₁₀ O ₁₀ S ₂ ·x C ₂ H ₄ O ₂	1019.24	(65)	mestastatic carcinoid tumors; vasoactive intestinal peptide-secretory tumors	nausea; diarrhea; loose stools; vomit-ing; abdominal pain; pain on injection
flutamide ^l (Eulexin)	[13311-84-7]	C ₁₁ H ₁₁ F ₃ N ₂ O ₃	276.21	(66)	metastatic prostatic carcinoma in combi-nation with LHRH agonist	diarrhea

^a See Figure 7.

^b ICI.

^c Marion-Merrill Dow.

^d Bristol-Myers Squibb.

^e Pharmacia.

^f Upjohn.

^g CIBA-GEIGY.

^h TAP.

ⁱ Sandoz.

^l Schering.

Aromatase inhibitors, which suppress estrogen production outside the ovaries, are useful for the treatment of tumors in postmenopausal women. Tamoxifen (54) is very well tolerated and is considered the drug of choice in post menopausal patients. The progestational agents medroxyprogesterone (59) and megestrol acetate (60) are used in the treatment of endometrial tumors to block overstimulation of the ovaries by estrogen. Megestrol acetate has been reported to have utility in reversing cachexia associated with cancer (31).

Miscellaneous Agents. Those chemotherapeutic agents, which do not fit into any of the classifications discussed, are listed in Table 7. Mitotane (67), a structural isomer of DDT, is used to induce chemical adrenalectomies in patients having adrenal cancer by reducing host levels of adrenocorticosteroids.

Table 7. Chemotherapeutic Agents

Drug (trade name)	CAS Registry Number	Molecular formula	Molecular weight	Structure number	Disease	Toxic effects
mitotane USP ^a (Lyso-dren)	[53-19-0]	C ₁₄ H ₁₀ Cl ₄	320.05	(67)	palliative treatment of inoperable adrenal cortical carcinoma	skin toxicity; vertigo; lethargy; somno-lence; anorexia; nau-sea; vomiting; diar-rhea
isotretinoin USP ^b (Accu-tane)	[4759-48-2]	C ₂₀ H ₂₈ O ₂	300.44	(68)	investigational drug	
sulofenur ^c	[110311-27-8]	C ₁ H ₁₅ ClN ₂ O ₃ S	350.82	(69)	investigational drug; refractory ovarian carcinoma response seen in Phase I	anemia; methemoglo-binemia
asparaginase ^d (Elspar)	[9015-68-3]				acute lymphocytic leukemia	hepatic, renal, and pancreatic toxicity; neurological effects; hypersensitivity reactions; clotting ab-normalities; nausea

^a Bristol-Myers Squibb.

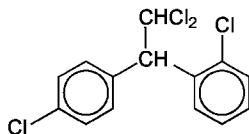
^b Hoffmann-La Roche.

^c Lilly.

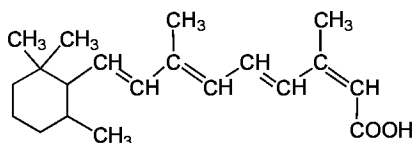
^d Merck Sharp & Dohme.

The retinoid isotretinoin (68) has been found to reduce the incidence of secondary malignancies in patients treated for head and neck cancer. In addition, the use of *trans*-retinoic acid in patients having M3 leukemia has been reported to induce complete, although temporary, remissions (32).

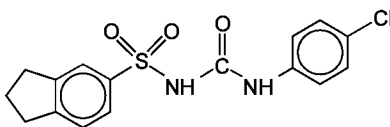
The novel agent sulofenur (69) has entered clinical trials based on its broad spectrum antitumor activity in tumor models, its unusual mechanism of action, and its lack of cross-resistance to other agents (33). In Phase I clinical trials, the drug was well tolerated and some clinical responses were noted.



(67)



(68)



(69)

The enzyme L-asparaginase is the only biological agent included in this review. Most normal cells are capable of synthesizing their own L-asparagine; leukemic cells are deficient in this regard. Use of the enzyme causes depletion of the exogenous L-asparagine necessary to the growth of the leukemia. Some remissions have been seen using this drug, however, they are usually transitory in nature because of the rapid emergence of resistance.

Toxicity

As a result of the life threatening nature of cancer and the general lack of therapeutically effective drugs for most cancers, doses of chemotherapeutic drugs in Phase I clinical trials are escalated until the emergence of a dose-limiting toxicity. The efficacy of these compounds in one or more tumor types is then established in Phase II–III clinical trials. The commonly observed dose-limiting toxicities include myelosuppression, gastrointestinal upset, and renal, hepatic, and cardiotoxicities.

The most common dose-limiting toxicity in cytotoxic chemotherapy is acute or cumulative suppression of bone marrow, ie, myelosuppression. To circumvent this, intermittent treatment schedules using suboptimal drug doses are often employed. Another approach involves either autologous, ie, derived from the same individual, or allogeneic, ie, derived from a different individual, bone marrow transplant accompanied by high dose therapy (34). Although therapeutic advantages have been achieved, patients are highly vulnerable to serious infections during the recovery period following reinfusion of bone marrow. When administered after infusion of the bone marrow, recombinant colony stimulating factors (CSFs) (14), granulocyte-macrophage-CSF (GM-CSF), and macrophage-CSF (M-CSF) stimulate the growth of white blood cells, particularly granulocytes, macrophages, and monocytes, hence shortening the recovery period so patients suffer fewer infections.

Cumulative organ toxicity also presents a significant obstacle for effective chemotherapy. In many cases, the severity of the toxicity impedes the broader use of an agent. Other specific toxicities are associated with specific agents, for example cardiotoxicity with adriamycin (32), renal toxicity with *cis*-platinum (28), and neurotoxicity with vincristine (49).

Toxicity Amelioration. Cancer researchers traditionally have not focused their attention on the question of toxicity amelioration. This is partly attributed to the lack of predictive animal models for human toxicities. For example, the preclinical rat model, used as a predictor of myelosuppression, has failed to predict myelosuppression in humans in clinical trials. In addition, reduction of one toxicity may result in the emergence of another, more serious problem. Research efforts to address the problem of toxicity amelioration has progressed in several directions. The three most prominent areas are analogue synthesis, chemoprotection, and drug targeting.

Analogue Synthesis. Two notable examples, in which analogues have greater therapeutic indexes than the parent drugs, have been identified in Phase I trials. These are carboplatin (29) and adozelesin (37) (35). Carboplatin's approval was based on its comparable efficacy to cis-platinum (28) and its more favorable toxicity profile, ie, reduced and delayed episodes of emesis, reduced ototoxicity, etc. On the other hand, adozelesin, a totally synthetic analogue of natural product CC1065, has demonstrated a similar potency and antitumor activity profile as its natural prototype but is devoid of the delayed death liability associated with the parent drug in animals (36).

Chemoprotection. The success of chemoprotection depends on a detailed biochemical knowledge of the drug target. The pharmacological and metabolic fate of the parent drug, its relationship to the observed organ toxicity, and how the observed toxicity can be prevented lessened by chemical intervention without affecting the antitumor activity of the parent drug are all important factors. Administering an antidote to the parent drug to minimize the specific drug toxicity to organs and the hematopoietic, ie, blood forming, system, is being studied in various cancer therapies. For example, leucovorin (9) rescue therapy has been used successfully in the clinic as an antidote to the toxic effects of high dose methotrexate (8). The antidote renders methotrexate ineffective against the newly recruited stem cells after its initial cytotoxic insult. Other combinations under active clinical study to demonstrate effectiveness of chemoprotection are ifosphamide (19) and mesna (20) for hemorrhagic cystitis (37); cis-platinum (28) and WR-2721 [20537-88-6] for nephrotoxicity and neurotoxicity (38); and adriamycin (32) and ICRF-187 [24584-09-6] for cardiotoxicity (39).

Drug Targeting. Site-specific drug delivery involving a variety of approaches has been pursued to address the issue of drug toxicity in chemotherapy (40). Prodrug synthesis and liposome encapsulation of cytotoxic drugs, eg, adriamycin (32), have preceded more modern drug targeting approaches. The advent of hybridoma technology to produce large quantities of monoclonal antibodies directed toward antigenic epitopes on human cancer cells has made possible several novel approaches to selective delivery of cytotoxic agents to human tumors. The three most actively pursued research areas in this vein are the use of monoclonal antibody-drug conjugates (41), a combination approach involving the use of a targeted antibody–enzyme complex followed by administration of a suitable prodrug of an anticancer agent (42); and antibody-targeted radionuclides with α and β -particle emitting properties (43). *In vivo* results for antibody targeted cytotoxics against human tumor xenografts in nude mice have been very encouraging and several institutions are planning clinical trials to establish the proof of principle for such approaches. The antibody targeted radionuclides approach, which has been widely used in cancer diagnosis, is also showing promise for therapeutic utility (44).

Drug Resistance

Despite dramatic advances in the treatment of several human malignancies including Hodgkin's lymphomas and leukemias, drug resistance remains a pressing issue in cancer chemotherapy. Acquired or induced drug resistance afflicts practically all classes of cancer agents. It usually is manifested clinically

subsequent to responsive therapy and cancer relapse following therapy often is fatal. The most recognized and studied mechanisms of drug resistance are attributed to multidrug resistance (MDR), gene amplification, DNA repair, topoisomerase II activity, and glutathione and metallothionein levels. Even with advances in understanding the biology and mechanism of drug resistance among different classes of antitumor agents, no real breakthrough appears imminent (45).

Research and clinical experience on drug resistance suggests that tumor cells are particularly adept at genetic selections leading to alterations in the structure, function, or synthesis of proteins involved in the antitumor drug action and detoxification. Multiple mechanisms of resistance have been shown to account for the resistance seen in the clinic (46).

Multidrug Resistance. MDR is characterized by reduced drug accumulation in tumor cells correlated with an enhanced drug efflux (47). This effect is common to a wide variety of cancer agents including the Vinca alkaloids, intercalators, and topoisomerase inhibitors. The drug efflux is attributed to the over expression of the MDR-1 gene, encoding a 170 kD glycoprotein (GP170) responsible for the energy (adenosine triphosphate) dependent nonspecific efflux of the drug from the MDR cells. In recent years, reversal of MDR by several classes of noncytotoxic agents, eg, verapamil [52-53-9], dipyridamole [58-32-2], progesterone [57-33-0], and dihydropyridine analogues, has been observed and studied at the preclinical level (48). Limited clinical trials are in progress to establish the validity of this approach. The exact mechanism of MDR reversal is not well understood but evidence suggests that these reversal agents either disrupt the efflux pump function or competitively inhibit drug binding to GP170 (49). The extent that MDR is responsible for the observed clinical resistance is being carefully monitored and evaluated.

Gene Amplification. This mechanism of drug resistance appears to be operative in drugs which act on *in vivo* enzymatic targets. For example, in the case of resistance to methotrexate (8), overexpression of the dihydrofolate reductase (DHFR) gene has been implicated. However, other mechanisms involving defects in drug uptake and polyglutamation also have been proposed and studied (50). Specifically, the multifactorial nature of methotrexate resistance represents a large therapeutic challenge. It is one example of how the heterogeneity of clinical resistance may be a serious problem.

DNA Repair. Resistance to alkylating agents, which constitute the bulk of chemotherapeutic agents, is ascribed to DNA repair and or detoxification processes (51). Resistance usually manifests itself as an overproduction of repair enzymes. Overproduction of O-6 alkylguanosine transferase, an enzyme responsible for repairing lesions in DNA, is observed in resistance to nitrosoureas, mitomycin C (25), and melphlan (23). In the case of resistance to cis-platinum (28), tumors have demonstrated elevated levels of glutathione and the enzyme glutathione S-transferase. Glutathione is involved in both DNA repair and drug detoxification processes. Reversal of cis-platinum resistance has been observed in cells pretreated with glutathione depleting agents such as buthionine sulfoximine [5072-26-4].

Investigational Approaches

Chemotherapy has been impacted significantly by a small number of selected antitumor agents. In the 1970s it was adriamycin (32) and in the 1980s it was cis-platinum (28) and etoposide (41). Based on its unique mechanism of action and its clinical performance to date, taxol (52) may be the most important chemotherapeutic agent of the 1990s (26). However, the quest for novel chemotherapeutics still continues, guided by both rational mechanism-based screening and more relevant animal tumor models for preclinical evaluations. Approaches under investigation include the search for novel noncytotoxic agents which induce differentiation of cancer cells (52), inhibit tumor metastasis (53), and control growth factors (54). The dramatic advances made in recombinant DNA and hybridoma technology has caused a resurgence in the science of immunotherapy (see IMMUNOTHERAPEUTIC AGENTS) (55); the use of cytokines such as the interferons, interleukin-2 [85898-30-2] (IL-2), and tumor necrosis factor [138415-31-3] (TNF) as activators of the human immune system is under active study. The use of immunomodulators, such as levamisole [14769-73-4], which stimulate and fortify the host's immunoreactivity toward tumors, also are being evaluated, but an unequivocal clinical demonstration of the effects of these biological response modifiers has not been made. In addition to use as selective drug delivery carriers, monoclonal antibodies are being employed as cytotoxic agents by the virtue of their natural effector mechanism (56). The clinical validity of all the above approaches are under careful scrutiny.

Resources are being marshalled to exploit and explore the possibility of cancer intervention at either the transcriptional or translational levels of gene activity. Specifically, as of 1992, antisense (RNA target) and antigene (DNA target) approaches (57,58) are being pursued at a number of institutions and several investigative therapies are pending FDA approval for initiation of human clinical trials.

Economics of Cancer Chemotherapy

The increased use of chemotherapy as a modality in the treatment of cancer has caused a corresponding increase in the market for anticancer agents. Table 8 lists the estimated 1990 worldwide sales for the most commonly utilized chemotherapeutic agents. Data for Japan are not included because of differences in medical and prescribing practices. Only a few anticancer drugs have achieved sales in excess of \$100 million per year and many of the drugs discussed herein sell less than \$10 million per year. Many of the approved drugs were introduced early on in cancer chemotherapy for the treatment of lymphomas and leukemias. Because of lack of patent coverage and the relatively small market size, these drugs are of relatively little commercial importance. Those agents which have achieved greater economic importance are newer, frequently used in combination chemotherapy, and of use in the treatment of solid tumors which comprise the bulk of reported cancer incidence. A number of the agents in clinical trials, such as taxol (52) and camptothecin analogues, are expected to have considerable economic impact based on activity in the treatment of the more common human malignancies, eg, lung, breast, colon, and ovary.

Table 8. Antitumor Drug Sales, 1990^a

Chemotherapeutic drug	\$ × 10 ⁶
<i>Antimetabolites</i>	
doxifluridine	112
fluorouracil	18
methotrexate	110
hydroxyurea	26
cytarabine	30
other	12
<i>Total</i>	308
<i>Alkylating agents</i>	
cis-platinum	192
carboplatin	191
mitomycin C	74
cyclophosphamide	54
ifosphamide	15
chlorambucil	13
thiotepa	13
melphalan	10
<i>Total</i>	562
<i>DNA interactive drugs</i>	
doxorubicin	150
epirubicin	110
mitoxanthrone	75
bleomycin	60

daunorubicin	18
Total	413
Topoisomerase inhibitors	
etoposide	260
Tubulin active dugs	
vincristine	30
vindesine	25
Total	55
Hormones ^b	
tamoxifen	540
leuprolide	170
flutamide	150
goserelin	112
medroxyprogesterone	92
estramustine	76
megestrol acetate	70
Total	1210

^a Estimated worldwide sales excluding Japan. Based on audited sales adjusted for under reporting. Sales of less than 10 million per annum not included.

^b Most hormonal agents are used for other indications. It is not possible to estimate usage for antitumor purposes.

In addition to the market for cancer chemotherapeutic drugs, there is also a growing market for biologicals such as the interferons, having combined 1990 sales of ~\$560million, and the colony stimulating factors, G-CSF, GM-CSF, etc. It is reasonable to expect an overall doubling of this market in the 1990s.

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CHEMOTHERAPEUTICS, ANTIMITOTIC.

See CHEMOTHERAPEUTICS, ANTICANCER.

CHEMOTHERAPEUTICS, ANTIMYCOTIC AND ANTIRICKETTSIAL.

See ANTIPARASITIC AGENTS, ANTIMYCOTICS.

CHEMOTHERAPEUTICS, ANTIPROTOZOAL.

See ANTIPARASITIC AGENTS, ANTIPROTOZOAL.

CHEMOTHERAPEUTICS, ANTIVIRAL.

See ANTIVIRAL AGENTS; IMMUNOTHERAPEUTIC AGENTS.

CHEMURGY

Chemurgy is defined as that branch of applied chemistry devoted to industrial utilization of organic raw materials, especially from farm products. A more modern and general definition for chemurgy is the use of renewable resources particularly biomass, usually plant or microbial material, for materials and energy (see FUELS FROM BIOMASS; FUELS FROM WASTE).

Chemurgy was really a social movement during the 1920s and 1930s when there were large surpluses of agricultural materials and severe economic problems in the farm areas. Using farm commodities as chemical or industrial raw materials was seen as a means of solving the economic problems (1–5). One significant outgrowth of this movement was the founding of the regional laboratories of the U.S. Department of Agriculture (USDA) which were considered to be chemurgic laboratories (6). Another success involved the making of strong paper from the fast-growing southern pine, leading to the foundation of the southern pulp (qv) and paper (qv) industry. This industry had been largely centered in the north and northeast and based on slower growing species.

Some of the early work on the manipulation of proteins (qv) arose out of the chemurgy movement. This technology has found application in synthetic meat production. Other technologies that may be classified as chemurgic include that of the cellulosic fibers, eg, rayon and cellulose acetate (see CELLULOSE ESTERS; FIBERS, CELLULOSE ESTERS); the recovery of turpentine and rosin from paper and pulping processes (see TALL OIL; TERPENOIDS); and the oils and fatty acids business (see CARBOXYLIC ACIDS; FATS AND FATTY OILS). Oils and fatty acids are used in a wide variety of chemical products including soap (qv) and detergents (see DETERGENCY; SURFACTANTS), cosmetics (qv), and coatings (qv).

Industrial Materials from Renewable Resources

One distinction that can be made in the area of chemurgy is between the use of natural products that are grown solely for industrial purposes as compared to those that are grown primarily for food. In the latter class, industrial materials may be either by-products from food production or substitutes for food uses when the commodity is in surplus.

Industrial Crops as Raw Materials. Trees are by far the largest commodity grown solely for industrial use. About two-thirds of the trees harvested are used for construction or structural uses (see BUILDING MATERIALS, SURVEY; WOOD) and about one-third are used for pulp and papermaking. About one-third of the pulp is made from residues of other timber conversion, such as trimmings and sawdust. Small quantities are used for fuel. Plywood is manufactured by peeling large strips from logs and then laminating with adhesives (qv). Still more complicated wood products are made from chips or slivers pressed together using binders such as phenolic resins (qv) (see WOOD BASED COMPOSITES AND LAMINATES) (7).

Other purely industrial crops include cotton (qv) and flax. Cotton is grown primarily for its fiber, although the protein and oil contained in the seed also contribute to farm income. Manufacture is simply a mechanical separation of the fiber from the seeds, followed by cleaning and mechanical processing into thread and ultimately textiles (qv). Flax is grown primarily for its seed which yields linseed oil, a drying oil used in coatings (qv) (see DRYING OILS). The fiber from flax grown in the United States is short and is used in certain types of fine papers such as cigarette papers. Longer flax fibers grown in other parts of the world are manufactured into the fine textile, linen.

There are relatively few other crops that are grown solely for industrial purposes. Among these are tung, a tree nut from which tung oil is produced, and castor from which is obtained castor oil (qv). Tung oil can be used as a drying oil in coatings. Wild crops being investigated for cultivation include jojoba, crambe, guayule, kenaf, and lesquerella.

Jojoba is a desert crop that gives a small bean containing about 50% of a wax, a fatty acid ester with a fatty alcohol. The only other large source of such a wax is sperm whale oil, traditionally used in fine lubricants (see LUBRICATION AND LUBRICANTS). Because the sperm whale is an endangered species, relatively little sperm whale oil is available and there is a large market for a substitute. Jojoba oil has been found to be usable for most of these applications. The jojoba oil is obtained by simply pressing the nut followed by conventional refining. Some jojoba oil is used in cosmetics (qv).

The problems with jojoba as a commercial crop are the usual ones of domestication and cultivation. It is a slow-growing plant, available only in the wild and therefore has very wide genetic variability. Efforts are underway to select the most promising variants and cultivate these as a crop in the southwestern United States deserts (7). A possible alternative for producing jojoba oil is to culture plant embryos in bioreactors (see CELL CULTURE TECHNOLOGY).

Guayule, potentially a source of natural rubber, is an unusual crop in that it has been an article of commerce in the past. Guayule grows wild in northern Mexico and the southwestern United States. When the leaves are milled in water, a latex is released that coagulates into natural rubber worms. These can easily be collected and relatively easily refined to give a product that is almost identical to the natural rubber from southeast Asia. During World War II there were several thousand acres of guayule planted in California and a small plant established to extract the rubber for military use. After the war,

however, this effort was shut down. Because it is believed that natural rubber trees may have reached their genetic potential and because these trees are in politically vulnerable areas, guayule may once more become an important crop (8). Guayule may also have use as a pesticide or coating (9,10).

Crambe was introduced to the United States in the 1970s. It is an oilseed, the oil of which is very high in erucic acid [112-86-7] (13-docosanoic acid), C₂₂H₄₂O₂. This oil can be used to provide industrial lubricants, especially those needed for the basic oxygen furnace process for making steel (qv). Crambe is grown in relatively small volume in the midwestern United States.

Kenaf is a grass fiber crop that has been proposed as a papermaking source. It is an annual crop and can be grown in many parts of the country. There have been agronomic problems with kenaf, primarily its vulnerability to nematode pests. Another problem is that kenaf is harvested once a year and must then be stored, usually as silage. There is some loss of the fiber in storage.

Lesquerella is an oilseed crop that has been mentioned as a potential industrial crop but is not yet grown in significant quantities. Castor beans have been a crop in the United States and provide a well-known lubricating product, castor oil [8001-79-4]. However, castor is grown only in small quantities and most of the castor used in the United States is imported from Brazil (11).

The economic disposal of oilseed meal presents a problem for almost every new oilseed. The large-volume oilseeds such as soy and peanut are particularly valuable because their oilseed meals contain large amounts of protein, which can be used almost directly for animal or even human food (see FEEDS AND FEED ADDITIVES). Many oilseeds contain toxic or other undesirable materials complicating use. For example, the crambe seed contains toxic and allergenic substances that must be removed before being fed to monogastric animals. A large part of the research on crops and oilseeds is devoted to upgrading the seed meal once the oil has been obtained by conventional pressing and solvent extraction methods. The seeds may be cooked first to release the oil. Cooking is often by direct contact with steam.

Food Crops as Raw Materials. Crops that are grown primarily for food can be used for industrial purposes when the crops are in surplus or are found to be unfit for their intended purpose. Historically, when agricultural surpluses are high, the distinction between industrial and food use is not significant. Additionally, there are large industries based on food commodities; eg, the corn and wheat starch separation processes to give starch (qv) used in paper sizing and textiles (see WHEAT AND OTHER CEREAL GRAINS). The starch is separated primarily by gravity in water slurries. Other starchy cereals could as easily be used, eg, milo or grain sorghum, rice, oats, and barley, although rice, oats, and barley are usually too valuable as food crops to be diverted to starch production. Potatoes and sweet potatoes also can be fractionated to give a very good starch product. Usually only the culls from fresh or processed potato manufacture are used for this purpose, but this is an important economic use because of the consumption of materials that would otherwise be wasted. Potato starch manufacture has suffered in the 1990s because the effluent from the process is a severe pollutant. Research has been directed to the utilization of this material, which contains high quality protein (12).

Oilseeds grown primarily for use in salad dressings, margarines, and cooking oils also produce an important by-product in the form of high protein meal. Historically, this meal was fed to animals but increasingly it is refined and fractionated for human consumption. Soy, in particular, is used to produce a large variety of specialized protein concentrates and isolates by various refining processes usually involving caustic solution and precipitation. A large quantity of soybean oil is also epoxidized to make an important plasticizer. Some other oilseeds that are important in the United States include rapeseed, sunflower seed, and safflower.

By-products from meat animals, which may be viewed as a food crop, are also commercially significant (see MEAT PRODUCTS). In addition to meat, each of these produces bones, trimmings, fat, hides, and in the case of sheep, wool (qv). The hides are turned into leather (qv) by tanning or are converted to commercial gelatin (qv) or other animal glue products. Inedible animal tallow may be exported and refined in foreign countries for edible use; some is added to animal feeds. A large amount is used in soaps and detergents or converted to fatty acids that may be refined or used as a mixture in soaps. Bristles from pork are used to a small extent in brushes. Animal hair is a waste product that creates disposal problems. Uses are still being sought for this material.

Wastes or By-products as Raw Materials. By far the largest volume of natural products for industrial use, aside from the forest products, are wastes or by-products of food processing (qv). The largest use of these wastes is as animal feeds. Because they are used rather than becoming a disposal problem, they are considered to be chemurgic products.

Wastes from the pulp and paper industry are finding increasing applications. These include lignin (qv) and tall oil (qv), as well as sugars in the form of sulfite waste liquor. Although the largest use of lignin [9005-53-2] is as a fuel in the pulping process, a wide variety of products can be made from it. Lignin, a polymer containing aromatic and phenolic functionalities, can be converted to a mixture of aromatic and phenolic compounds by hydrogenation. These compounds occur in large variety and only relatively small quantities of any one substance can be isolated. In this respect, converted lignin is more like coal tars from coking than fractions from crude oil. Lignin is used in dispersants (qv), adhesives (qv), additives to drilling muds (see PETROLEUM, DRILLING FLUIDS AND OTHER OIL RECOVERY CHEMICALS), and fillers (qv).

Tall oil [8002-26-4] has been referred to as the largest and fastest growing source of extractives such as turpentine and resin. It can be refined to give tall oil fatty acids (see CARBOXYLIC ACIDS) and tall oil pitch as well as resins. These fatty acids compete with fatty acids from vegetable sources for many of the same industrial markets.

Sulfite waste liquor from the pulping industry contains a large amount of hydrolyzed sugars. Some sulfite waste liquors are now being fermented to give both ethanol (qv) and single-cell protein in the form of yeast (see FOODS, NON CONVENTIONAL; YEASTS).

The trimmings and slash from forest operations historically have been left in the forest but increasingly these materials are being used in much the same way as higher quality timber, primarily for pulping or chipping. Agriculture produces large amounts of wastes in the form of animal manures, branches, stems, stalks, and straws. These wastes also have historically been returned to the land. Changing patterns of production have made it less convenient to use these for their fertilizer value, however, and have aggravated the pollution problem they create. It is possible to recycle animal wastes as animal feed because a large amount of nutritive value is retained in the waste. The enormous volume of animal waste is also being considered as a potential energy source, probably by anaerobic fermentation to produce methane [74-82-8] (13). Other agricultural wastes, such as straw, have been considered for pulp and papermaking and for digestion to produce fuel. They are also candidates for hydrolysis of the cellulose content to produce glucose (see CARBOHYDRATES). Hydrolysis can be acidic or enzymatic, and products are primarily ethanol but can include other chemicals (14–16).

The processing of agricultural products to make foods and feeds yields wastes that have traditionally been considered valueless. Constraints on dumping make it necessary to consider these wastes as raw materials. A good bit of research into uses for wastes has been motivated primarily by environmental considerations. For example, kraft black liquor, sulfite waste liquor, and other dilute streams from pulp and papermaking are potential fermentation substrates because of the dissolved sugar, which is also the material that is the most serious pollutant. Cereal grain milling produces a variety of fractions that have found historic uses in animal feeds. Research has been conducted on isolation of protein concentrates from these materials for upgrading as human foods.

Cellulosic materials, such as farm wastes, can be upgraded for animal feed by simply bringing them into contact with ammonia (qv). The cellulose swells and is made more digestible, and at the same time some ammonia nitrogen, which is a nutrient for ruminants, is left behind. Supercritical ammonia improves susceptibility to enzymatic hydrolysis (17).

Some of the forest wastes and pulp and paper processing wastes contain dilute concentrations of important acids such as acetic acid (see ACETIC ACID AND DERIVATIVES) and solvents such as methanol (qv), formed from the wood in the high temperature digestion of pulping. Although these waste streams have been discarded as too dilute for commercial recovery, it is increasingly attractive to use materials from such processes as liquid–liquid extraction (see EXTRACTION, LIQUID LIQUID), or adsorption (qv) on charcoal followed by steam stripping can be employed to remove and concentrate the organic chemicals.

Processing Methods

The largest class of processes applied to farm commodities are separations, which are usually based on some physical property such as density, particle size, or solubility. For example, the milling process for cereal grains involves size reduction (qv) followed by screening to yield products that have varied concentrations of starch, fiber, and protein. Milling of water slurries is practiced to obtain finer separation of starch, fiber, protein, and oil.

Solubility is used in the refining of oilseed meals to give protein isolates and concentrates (18). Proteins are highly soluble in basic solutions and the

processes of isolation and concentration involve repeated dissolution, physical separation by centrifuging or filtration, followed by precipitation of the protein. Solubility properties are used to extract oil from oilseed meals. The usual solvents are light hydrocarbons such as hexane. There is also some separation on the basis of volatility such as the distillation of essential oils, the recovery of solvent from edible oils, and the distillation of esters of fatty acids.

In general, the separation processes used in chemurgy are relatively simple. In contrast, the chemical reactions that are possible with chemurgic materials can be very sophisticated. The chemistry involved is often reductive because so many of the chemurgic materials, such as cellulose and starch, are carbohydrates. Also important are the carboxylic acids and the amine groups of protein. Reactions such as the esterification of sugar (qv) and the epoxidation of soy oil are of commercial significance. Also important are the acetylation of cellulose to make it soluble for subsequent spinning into fibers, and the solubilization of starch and cellulose as xanthates (qv).

Increasingly, biochemical transformations are used to modify renewable resources into useful materials (see MICROBIAL TRANSFORMATIONS). Fermentation (qv) to ethanol is the oldest of such conversions. Another example is the cell-free enzyme catalyzed isomerization of glucose to fructose for use as sweeteners (qv). The enzymatic hydrolysis of cellulose is a biochemical competitor for the acid catalyzed reaction.

Uses

A rather impressive list of materials and products are made from renewable resources. For example, per capita consumption of wood is twice that of all metals combined. The cellulosic fibers, rayon and cellulose acetate, are among the oldest and still relatively popular textile fibers and plastics. Soy and other oilseeds, including the cereals, are refined into important commodities such as starch, protein, oil, and their derivatives. The naval stores, turpentine, pine oil, and resin, are still important although their sources are changing from the traditional gum and pine stumps to tall oil recovered from pulping.

Textile fibers are made from chemurgic materials such as cotton, rayon, linen, and wool (qv).

The transportation industry utilizes chemurgic materials such as fuels, lubricants, and coatings. Ethanol is added to gasoline to form gasohol and sold as a motor fuel (see ALCOHOL FUELS). Additionally, vegetable oils can be used as fuels for diesel engines. Lubricants of the 1990s are subject to higher stress than previously because of antipollution devices and smaller engines. Whereas historically castor oil (qv) has been an important automobile lubricant, its application in that use is now small. Biomass materials can also be pyrolyzed to produce oils and fuel gas (19–22).

The housing industry represents a large market for chemurgic materials. Wood is the cheapest material of construction generally available and has the advantage of being a good thermal insulation material. In addition to use as foods, large numbers of food additives can be made from agricultural products; for example, modified starches, cellulose gums, flavors and aromas from turpentine, and other less obvious applications (see FLAVORS; GUMS; PERFUMES; TERPENOIDS). Also, rosin can be used to produce resins that compete directly with resins from petroleum (see HYDROCARBON RESINS; RESINS, NATURAL).

The fermentation industry is based almost exclusively on renewable materials in the form of molasses, starch, etc. Most products are of very high value and relatively low volume such as antibiotics (qv) (23).

Industrial alcohol (ethanol) may be made by fermentation or by hydration of ethylene. Beverage alcohol must be made by fermentation (see BEVERAGE SPIRITS, DISTILLED; BEER; WINE). Since 1973, increases in the price of ethylene have made industrial alcohol by fermentation again competitive at ca \$0.25 L (\$1 gal). Fermentation plants that had been shut down for many years have been reopened and are likely to gain an increasing portion of this business. However, the efficiency of conversion of glucose to ethanol is less than 50% because so much carbon dioxide is also made. The state governments in the grain growing mid-western United States have revived the idea of ethanol as a fuel and have passed legislation providing economic incentives for the use of fermentation-based ethanol as a gasoline additive to form gasohol as a motor fuel (see GASOLINE AND OTHER MOTOR FUELS) (24). An extensive ethanol fuel program based on sugar cane has been developed in Brazil.

Grain that is usable as food or feed is an expensive substrate for this fermentation process. A cheaper substrate might be some source of cellulose such as wood or agricultural waste. This, however, requires hydrolysis of cellulose to yield glucose. Such a process was used in Germany during World War II to produce yeast as a protein substitute. Another process for the hydrolysis of wood, developed by the U.S. Forest Products Laboratory, Madison, Wisconsin, uses mineral acid as a catalyst. This hydrolysis industry is very large in the former Soviet Union but it is not commercial elsewhere.

More recently, interest has developed in the use of enzymes to catalyze the hydrolysis of cellulose to glucose (25–27). Domestic or forest product wastes can be used to produce the fermentation substrate. Whereas there has been much research on alcohol fermentation, whether from cereal grains, molasses, or wood hydrolysis, the commercial practice of this technology is primarily for the industrial alcohol and beverage alcohol industries. About 100 plants have been built for fuel ethanol from corn, but only a few continue to operate (28).

Generating energy from biomass in some form is a use of chemurgic materials. The direct combustion of plant materials or fermentation to yield methane for combustion have both been topics for research. Wood has been burned as a fuel for many years and generates more energy in the United States than do nuclear sources. The bulk of this use was in forest products industries where wood wastes were burned on-site for energy generation. Small-scale anaerobic fermentations of agricultural wastes to yield methane are practiced but large-scale processes have not yet been built, except in sewage treatment plants to dispose of sludge (see WASTES; WATER, SEWAGE).

Potential for Renewable Resources

A 1976 study (29) on renewable resources for industrial materials emphasized forest products because these represent the largest volume of renewable resources; however, this study also considered such things as special crops, animal by-products, and marine by-products. The conclusion was that competition between chemurgic material and one from a nonrenewable resource would be resolved by economics and that there were significant energy economies in the use of renewable resources for a great many materials. One exception was the cellulosic fibers, acetate and rayon, which consume relatively large amounts of energy. This study was summarized (30).

The potential for converting wood to plastics has been considered (31). Because plastics and polymers are among the largest volume industrial materials, the ability to convert chemurgic or renewable resources to these substances would clearly be significant. With few exceptions, industrial polymers and plastics are based on petrochemicals (see FEEDSTOCKS, PETROCHEMICALS AND FEEDSTOCKS). Each of these important building blocks, primarily ethylene (qv), propylene (qv), and benzene (qv), could in theory be obtained from trees or agricultural wastes by an integrated series of processes involving the hydrolysis of cellulose using either mineral acids or enzymes. Wood or agricultural waste converted to glucose can then be converted to ethanol, which in turn can be dehydrated to ethylene or used to make butadiene (qv). These olefins are necessary for a large class of polymers, including the polyolefins and styrene (qv) (see OLEFIN POLYMERS; STYRENE PLASTICS).

Hydrogenolysis of glucose, sucrose, starch, or cellulose can lead to glycerol (qv) and propylene glycol (see GLYCOLS) and lignin can be hydrogenated or hydrolyzed to yield large fractions of aromatics and phenolics which in principle could be used as feedstocks. Thus the entire petrochemical base of polymers could be replaced by lignocellulosic materials (32). Phenols from lignin can be made competitively if the price of petrochemical phenol (qv) is high enough. The by-products of lignocellulosic chemical conversions would presumably include extractives and the products of acid catalyzed degradation of glucose. These latter products, such as hydroxymethylfurfural, levulinic acid, and, from the degradation of pentoses, furfural, could be recovered for use in the chemical industry (see FURAN DERIVATIVES).

Many problems need to be solved before chemurgic materials can be economically used as feedstocks. Among these problems are the recovery, purification, and fractionation of the diverse materials. However, none of these problems are insurmountable. Serious concerns are the supply of the raw material, the relative costs of competitive materials, and competition with other uses for the raw materials. Competition is particularly significant because materials, such as wood, could easily be used in many cases for pulping or even higher value products, such as structural timber. Municipal solid waste offers a substitute raw material with few other uses (33).

The future of chemurgy is interconnected with the economic future of energy, environment, and food. Several scenarios exist for future sources of energy and materials. Some involve the use of nuclear or solar energy (qv) leaving coal and oil available for chemicals and transportation fuels. Some involve

the use of coal (qv) and oil (see PETROLEUM) almost exclusively for energy. Materials would then come from other sources and this would place great demands on chemurgic processes involving wood, foliage (34), or other by-products. However, it is most likely that the competition of chemurgic materials with synthetic ones will be settled in the marketplace.

Another substitution taking place is the use of vegetable protein for meat protein. Whereas this substitution does not directly affect any nonrenewable resource, there are consequences for the increased availability of by-products of vegetable protein processing. Additionally, a rather complex competition exists among the various vegetable oils, animal tallow, and hydrocarbons. Most of the vegetable oils are essentially interchangeable although the processes needed to make them useful vary depending on the type of contamination they may contain. An example of this is the removal of color from palm nut oil. Tallow can be fractionated to give materials equivalent to vegetable oils as well as higher melting materials. Triglycerides in fats, oils, and tallows can be used for many of the same purposes as hydrocarbons such as lubrication, as a fuel, or, as in the past, for illumination. However, as meat production declines or stabilizes, the relative amount of tallow available also declines.

The economic balance must be considered between recovery, reuse, and modification of a waste material or by-product and its disposal. The future is expected to bring increases in the practice of recycle, recovery, modification, and upgrading of wastes of all sorts, and a reduction in disposal by incineration (qv), biochemical oxidation, or discharge to the environment (see RECYCLING).

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CHICLE.

See GUMS.

CHIPS.

See INTEGRATED CIRCUITS; SILICON.

CHLORAL.

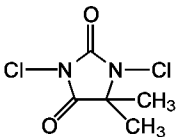
See HYPNOTICS, SEDATIVES, ANTICONVULSANTS.

CHLORAMINES AND BROMAMINES

N-Halamines are inorganic and organic compounds in which halogen is attached to nitrogen. They have both research and industrial importance. The *N*-halogen bond is formed by reaction of an amine, imine, amide, or imide with halogen, hypohalous acid, or hypohalite. Numerous *N*-fluoramines have been prepared and are used as selective fluorinating agents. Iodamines are the least stable and least studied. Only the chloro and bromo derivatives are of commercial importance. The chemistry of chloramines and bromamines is diversified not only because nitrogen and halogen act as reaction sites but also because of the different modes by which these functionalities react. In aqueous solution, chloramines and bromamines undergo hydrolysis to varying degrees forming HOCl and HOBr. Thus these *N*-halamines can be considered as halogen release agents and many find use in bleaching, disinfecting, and sanitizing applications. Others, such as the halogen derivatives of ammonia, are important because they are industrial process intermediates (monochloramine) or of significance in water treatment (mono-, di-, and trichloramine).

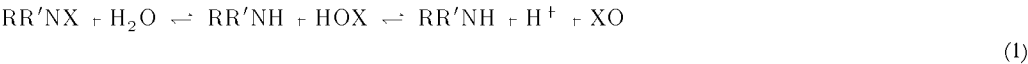
Properties

Available Halogen. The available halogen in an *N*-halamine is the percent N—X halogen expressed in terms of equivalent molecular halogen, ie, it is a measure of the oxidizing capacity in terms of elemental halogen. For example, the available chlorine (av Cl₂) in trichloroisocyanuric acid (TCCA) is 91.5%. The following equation illustrates the concept of available halogen, wherein halamines liberate free halogen upon acidification, one mol of halogen being liberated for each N—Cl or N—Br bond: RR'NX + HX → RR'NH + X₂. In water treatment, a distinction is made between free available chlorine (FAC) and combined available Cl₂ (CAC). Historically, FAC has referred to HOCl + ClO⁻, and CAC to ammonia chloramines and other slightly hydrolyzed N—Cl compounds. FAC reacts with *N,N*-dimethyl-*p*-phenylenediamine (DPD), whereas CAC requires the presence of acidic KI. Although TCCA exists predominately in the form of chloroisocyanurates in aqueous media, it analyzes essentially as FAC because the hydrolysis reactions are so rapid. Thus TCCA is a reservoir of HOCl, representing potential FAC. By contrast to TCCA, the first chlorine of 1,3-dichloro-5,5-dimethylhydantoin (1) analyzes as FAC but the second as CAC.



(1)

Hydrolysis. Halogen in *N*-halamines is formally positive, ie, the oxidation state is +1. *N*-Halamines hydrolyze yielding hypohalous acid, which ionizes to hypohalite ion depending on pH (see CHLORINE OXYGEN ACIDS AND SALTS DICHLORINE MONOXIDE, HYPOCHLOROUS ACID, AND HYPOCHLORITES).



The extent of hydrolysis is a function of the polarity of the N—X bond, which is determined by the electronegativity of X and the nature of the other substituents; the lower the polarity the lower the extent of hydrolysis. In general, electron-donating groups retard hydrolysis whereas electron-withdrawing groups enhance it. Presence of charges and steric and resonance effects also influence the extent of hydrolysis. Bromo compounds hydrolyze to a greater extent than chloro compounds.

The equilibrium expressions for the hydrolysis reactions (eq. 1) follow; *K_a* and *K_w* are the ionization constants of HOX and water, respectively.

$$K_{HOX} = \frac{[RR'NH][HOX]}{[RR'NX]} \tag{2}$$

$$K_{OX} = \frac{[RR'NH][OX^-]}{[RR'NX][HO^-]} = \frac{K_{HOX} K_a}{K_w} \tag{3}$$

Equation 2 rearranged for the concentration of HOX, shows that the percent hydrolysis increases with decreasing concentration of *N*-halamine.

$$[HOX] = K_{HOX} \frac{[RR'NX]}{[RR'NH]}$$

However, as HOX is consumed, hydrolysis is retarded because of build-up of free amine. Consumption of hypohalous acid through reaction with HX can result in formation of elemental halogen: HOX + H⁺ + X⁻ ⇌ X₂ + H₂O (1–3). The tendency for halogen formation is much greater for HOBr and becomes significant at moderately acidic pH.

In the case of multiple halogen atoms, the hydrolysis constant K_h decreases significantly for successive halogens. For example, in the case of trichloroisocyanuric acid, K_h ranges from 1.6×10^{-2} to 8.5×10^{-4} for the first to the third chlorines (4). The presence of negative charge also reduces K_h significantly, eg, 1.2×10^{-3} and 3.2×10^{-4} for dichloroisocyanuric acid and ion, respectively.

Bleaching. A K_h of 10^{-4} is sufficient to provide acceptable performance which approaches that of hypochlorite bleaches. Commercial products such as bleaches, dishwasher detergents, and hard surface cleaners are formulated with alkaline ingredients such as polyphosphates, silicates, etc, so that chloramines initially hydrolyze to hypochlorite during use. Consumption of hypochlorite forms acidic compounds by reaction with soil causing the pH to drop resulting in formation of some HOCl which increases the bleaching rate. In laundry bleaching this can result in lowering of the tensile strength of the fabric. In bleaching applications, four variables are important including pH, temperature, contact time, and concentration. In commercial laundries, optimum pH and temperature are in the 10.2–11.0 and 66–71°C ranges, respectively.

Disinfection. The disinfection efficiency of *N*-halamines is related to the extent of hydrolysis to hypohalous acid. For example, NH_2Cl ($K_h \sim 10^{-12}$) is a poor bactericide compared to HOCl (5). By contrast, monochloroisocyanurate ($K_h \sim 10^{-6}$) exhibits good bactericidal properties (6). Since hypohalous acid is a much more effective disinfectant than hypohalite, pH affects the disinfection efficiency. The fraction of hypohalous acid for aqueous chlorine and bromine is $\text{HOX} / (\text{HOX} + \text{XO}^-) = 1 / ([\text{H}^+] / K_a + 1)^{-1}$, where the $\text{p}K_a$ s of HOCl and HOBr at 25°C are 7.54 (2) and 8.70, respectively (7). The $\text{p}K_a$ values indicate that significant fractions of HOBr acid exist at higher pH compared to HOCl, with 50% neutralization pH of 8.7 and 7.54, respectively. Increasing the temperature increases the extent of dissociation of hypohalous acids. For HOCl, $\text{p}K_a$ varies with temperature (K) as follows: $\text{p}K_a = 0.0253T + 3000 / T - 10.0686$ (2).

For optimum disinfection in swimming pools, the pH is maintained in the 7.2 to 7.6 range where HOCl represents 69–47% of the FAC. By contrast, the HOBr fraction varies from 97 to 93%. Nevertheless, the bactericidal effectiveness of HOCl is greater than that of HOBr below pH 8 on a molar basis (8). However, above pH 8 the superiority of HOCl is overcome by the fact that the concentration of ClO^- exceeds that of HOCl above pH 7.5, whereas the concentration of HOBr still exceeds that of BrO^- up to pH 8.7. Hypochlorous acid is a better viricide than HOBr, but HOBr is more effective against certain algae (9).

Although pH determines the ratio of hypohalous acid to hypohalite ion, the fraction of the total available halogen present as HOX is dependent on K_h of the halamine as well as the concentration of excess amine. In the case of chloroisocyanurates, which are the most widely used *N*-chloramine disinfectants in swimming pools and spas, the extent of hydrolysis at 1 ppm av Cl_2 (as monochloroisocyanurate) is ~34% but only ~1% when 25 ppm cyanuric acid is added (4). Nevertheless, effective disinfection can still occur with chloroisocyanurates if a sufficient FAC is maintained, eg, 1–3 ppm. The observed reduction in disinfection rate because of cyanuric acid (6) has been shown to be directly related to the concentration of HOCl formed by hydrolysis of chloroisocyanurates (10).

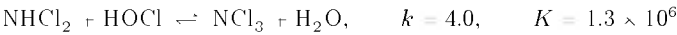
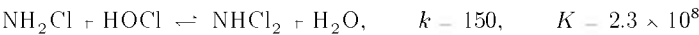
In studies with so-called soft *N*-chloramines, the following factors were shown to significantly influence antimicrobial activity: (1) the aliphatic chain length; (2) the degree of chlorination of the N atom; and (3) the nature of a positive charge (11).

Thermal and Photostability. Some chloramines and bromamines exhibit the lack of stability expected of compounds with bonds between two strongly electronegative elements. Decomposition kinetics can be rapid and energetic and explosive in many cases, eg, NCl_3 and NBr_3 . However, these compounds can be handled safely in dilute organic or aqueous solution. In general, bromamines are less stable than chloramines. A significant factor responsible for degradation of *N*-haloorganics is dehydrohalogenation across the carbon–nitrogen bond. Therefore, it is essential to stability to replace hydrogen atoms on the carbon adjacent to nitrogen with alkyl or other functional groups. Commercial organic *N*-bromamines and *N*-chloramines have good stability, which is a function of temperature, moisture, and impurities. For example, sodium dichloroisocyanurate and trichloroisocyanuric acid lose substantially less than 1% of their av Cl_2 in a year when stored at moderate temperature and th.

When chlorine is employed for outdoor swimming pool sanitation, it is relatively rapidly decomposed by sunlight. Isocyanuric acid stabilizes chlorine by formation of photostable chloroisocyanurates (12). By contrast, bromine is not stabilized by isocyanuric acid.

Inorganic Chloramines and Bromamines

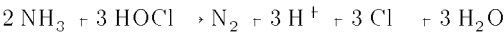
Chloramines are formed by electrophilic attack on ammonia nitrogen via a series of bimolecular reactions, where $k \text{ (M}^{-1} \text{s}^{-1}\text{)}$ and $K \text{ (M}^{-1}\text{)}$ are the formation and equilibrium constants at 25°C and $\mu = 0.50 \text{ M}$ (13–18).



The lack of dependence on ionic strength in the first reaction indicates that it occurs between neutral species. Mono- or dichloramine react much slower than ammonia because of their lower basicities. The reaction is faster with Cl_2 because it is a stronger electrophile than with HOCl. The degree of chlorination increases with decreasing pH and increasing $\text{HOCl}:\text{NH}_3$ mol ratio. Since chlorination rates exceed hydrolysis rates, initial product distribution is determined by formation kinetics. The chloramines hydrolyze very slowly and only to a slight extent and are an example of CAC.

Similar reactions occur with ammonia and HOBr (19–25), but since HOBr is a stronger electrophile than HOCl, formation rates are faster. Because of rapid bromine transfer between bromamines, equilibrium concentrations of the respective bromamines are obtained quickly. Monobromamine predominates at basic pH at high N:Br ratios. Below pH 8.5, NHBr_2 and NBr_3 predominate. Tribromamine formation is favored at lower pH and higher Br:N ratios. The bromamines are less stable than chloramines but are better disinfectants.

At environmental pH 6–9, ammonia is oxidized to nitrogen by the following overall reaction (26,27).



Some nitrate is also formed, thus the $\text{HOCl}:\text{NH}_3$ stoichiometry is greater than theoretical, ie, ~1.7. This reaction, commonly called breakpoint chlorination, involves intermediate formation of unstable dichloramine and has been modeled kinetically (28). Hypobromous acid also oxidizes ammonia via the breakpoint reaction (29). The reaction is virtually quantitative in the presence of excess HOBr. In the case of chlorine, little or no decomposition of NH_3 occurs until essentially complete conversion to monochloramine. In contrast, oxidation of NH_3 commences immediately with HOBr because equilibrium concentrations of NH_2Br and NHBr_2 are formed initially. As a result, the typical hump in the breakpoint curve is much lower than in the case of chlorine.

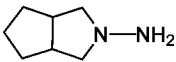
Monochloramine. The most important of the ammonia halamines, monochloramine [10559-90-3], is prepared by reaction of equimolar solutions of NH_3 and ClO_2 (30). The pure compound decomposes even at low temperatures (31). Concentrated aqueous NH_2Cl (~70 mol %) is a colorless liquid with a strong pungent odor, that decomposes at 50°C to N_2 , Cl_2 , and NCl_3 (32). However, it is relatively stable when employed in dilute solutions of ether or water. For kinetic studies, stable aqueous chloramine solutions are formed quantitatively under efficient mixing conditions if NH_3 is in slight excess and $\text{pH} > 8.5$ (15). Monochloramine is the least odorous of the chloramines; the odor and taste threshold is 5 ppm. Chloramination, ie, *in situ* NH_2Cl formation, is increasingly employed to disinfect public water supplies to reduce trihalomethane (THM) formation (33). Since direct transfer of Cl from NH_2Cl to organonitrogen compounds can occur (34–36), this can cause a problem in non-nitrified effluents from wastewater that contain significant amounts of amino acids because *N*-chloroamino acids are even poorer disinfectants than chloramines from ammonia (37).

The chemistry of NH_2Cl involves chlorination, amination, addition, condensation, redox, acid–base, and decomposition reactions. Monochloramine

adds to ketones forming vicinal chloroamines and condenses with aldehydes giving *N*-chloroimines. Excess base decomposes NH₂Cl to NH₃ and N₂. Reaction of equimolar amounts of NH₂Cl and caustic with excess NH₃ is the basis of the industrial-scale production of hydrazine [302-01-2].



Monochloramine is also used in organic synthesis for preparation of amines, substituted hydrazines, etc. For example, reaction of NH₂Cl with 3-azabicyclo[3.3.0]octane [5661-03-0] yields *N*-amino-3-azabicyclo[3.3.0]octane [54528-00-6], a pharmaceutical intermediate (38).



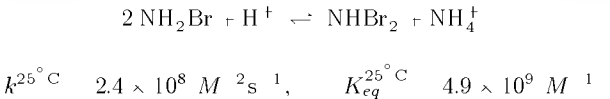
Dichloramine. The least stable chloramine, dichloramine [3400-09-7], has not been prepared in pure form. However, it has sufficient stability in dilute organic or aqueous solutions for determination of some physical and chemical properties. It has a pungent odor and can impart an odor or off-taste to water at concentrations above 0.8 ppm. Dichloramine can be produced by reaction of HOCl with a slight excess of NH₃ in the pH range 4–7 or by disproportionation of NH₂Cl at pH 3.5–4.0:



Prepared by the latter route, decomposition is ~10% in 24 h. This reaction involves direct Cl transfer to NH₂Cl via the intermediate NH₃Cl⁺; NH₂Cl hydrolysis playing little or no role. The presence of NH₄⁺ improves stability by reacting with HOCl which tends to increase decomposition (39). Trichloramine also increases decomposition, whereas NH₂Cl has little effect. Dichloramine is useful for preparation of diazirine (40).

Trichloramine. Nitrogen trichloride, trichloramine [10025-85-1], the only stable pure ammonia halamine, is a shock-sensitive dense yellow liquid (bp 71°C) with a volatility similar to chloroform. In the gas phase it can be completely decomposed to N₂ and Cl₂ by spark initiation at concentrations of only a few % in air. At higher concentrations, the decomposition is propagated by flame, exhibiting the characteristics of explosion and eventually detonation. Trichloramine has a pungent odor and is a lachrymator. Its solubility in water at room temperature is ~2000 ppm (12). It is the most irritating of the chloramines and can impart an odor or off-taste to water at concentrations above only 0.02 ppm. Trichloramine is prepared by reaction of (NH₄)₂SO₄ with Cl₂ (41) or HOCl with ammonia in a 3 to 1 molar ratio at pH 3–4. Dilute solutions are relatively stable when protected from light and volatilization (42). It decomposes in basic solution to N₂ and ClO⁻ via intermediate formation of dichloramine: 2 NCl₃ + 6 HO⁻ → N₂ + 3 ClO⁻ + 3 Cl⁻ + 3 H₂O. Reaction of NCl₃ with olefins gives high yields of vicinal dichlorides via a radical mechanism (43). When catalyzed with AlCl₃, trichloramine acts as an aminating agent towards various organic substrates (44). Trichloramine has been used as a bleaching agent for flour and in manufacture of paper and as a fungicide for treatment of fruit.

Monobromamine. In organic solvents monobromamine [14519-10-9] is dark violet. It is formed rapidly and quantitatively by reaction of NH₃ and Br₂ in organic or aqueous media; *k*(H₂O/HOBr) = 7.4 × 10⁷ M⁻¹s⁻¹ at 25°C. The solutions are relatively unstable, decomposing as follows: 2 NH₂Br + 4 HO⁻ → N₂ + 2 Br⁻ + 4 H₂O (19). In aqueous media the decomposition increases with pH and Br:N mol ratio. For example, at pH 9 and Br:N = 0.02, the decomposition rate is about 30% h, whereas at Br:N = 0.002 the decomposition rate is 5% h. Monobromamine disproportionates to dibromamine.



Dibromamine. Dibromamine [14519-03-0] can be prepared in ether by reaction of Br₂ with a slight excess of NH₃ (45). The solution has a strawberry-yellow color and a sharp irritating odor. Although stable at -70°C it decomposes rapidly at >0°C. In aqueous media, *k*(HOBr) = 7.0 × 10⁶ M⁻¹s⁻¹ at 25°C. Best yields are obtained in the 5.5–6.3 pH range and a Br:N mol ratio of ~0.05 (19). Dibromamine is less stable than NH₂Br, eg, at pH 7.2 and Br:N = 0.34, >90% decomposition occurs in less than 5 min.

Tribromamine. Pure solid nitrogen tribromide [15162-90-0] is deep red and explodes even at -100°C (46). Formation of NBr₃ in aqueous media is favored by lower pH and an excess of Br to N (19,29). At pH 4.5 and a Br:N molar ratio of 2.5, essentially complete conversion of Br to NBr₃ occurs. Tribromamine is more stable than dibromamine. At pH 4.5 it decomposes at 5% h.

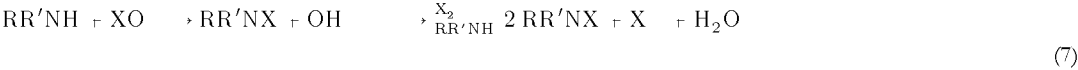
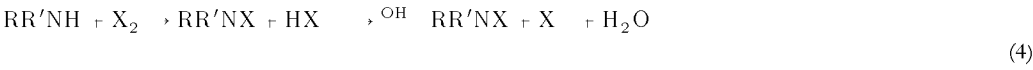
Sulfamates and Imidosulfonates. Sodium, potassium, and bromine analogues of *N*-chlorosulfamic acid, [17172-27-9] ClHNSO₃H, and *N,N*-dichlorosulfamic acid, [17085-87-9] Cl₂NSO₃H, have been prepared and the kinetics of chlorination of sulfamic acid have been studied (13). Dichlorosulfamate is relatively stable in dilute buffered aqueous solution (47) but is decomposed by excess av Cl₂ forming NCl₃ and H₂SO₄ (48). Sulfamic acid was once used as a stabilizer for av Cl₂ in swimming pools (49). However, its use was discontinued because of the poor bactericidal properties of mono- and dichlorosulfamate (50). *N*-Chlorosulfamates are useful in dishwashing compositions (51,52), textile bleaching (47,53,54), and vat or sulfur dyeing (55). *N,N*-Dichlorosulfamate can be used as a bleach (51,55) and disinfectant (47,54,56). *N*-Chloroimidodisulfonates, eg, sodium *N*-chloroimidodisulfonate, [6700-32-7] ClN(SO₃Na)₂, can be used for fabric bleaching and stain removal (57,58).

Other Inorganic Compounds. The cyclic sodium trichloroimidometaphosphamate, [67651-15-4] NaH₂(ClNPO₂)₃, 52% av Cl₂, was once employed as a bleaching and sanitizing agent (59). *N*-Halosulfinylamines, O=S=NX, can be prepared by reaction of SOX₂ with [(CH₃)₃Si]₂NI (60). They are thermally stable liquids at room temperature but react explosively with water. *N*-Halo-*S*, *S*-difluorosulfilmines, F₂S=NX, are formed when SF₄ and [(CH₃)₃Si]₂NX react in a 1:1 mol ratio, whereas, a 1:2 mol ratio yields *N,N'*-dihalosulfurdiimides, XN=S=NX (61). *N,N'*-Dibromosulfurdiimide is shock sensitive. *N*-Chloroimidodisulfuryl fluoride [15588-41-7], (FSO₂)₂NCl, rearranges photochemically to a tetrasubstituted hydrazine and adds to unsaturated molecules such as olefins, CO, and cyanogen halides (62). *N*-Chloroimidodisulfuryl fluoride [13816-63-2], F₂S(O)=NCl, prepared by chlorination of (CH₃)₃SiN=SOF₂, adds photochemically to olefins (63). Pentafluorosulfonyl-*N,N*-dichloramine [22650-46-0], SF₅NCl₂, bp 64°C, formed by reaction of ClF with N≡SF₃, is shock sensitive, unstable at 80°C, and hydrolyzes slowly (64). In the presence of SF₅Cl it photolyzes to the novel hydrazine (SF₅)₂NN(SF₅)₂ (65).

Organic Chloramines and Bromamines

Organic chloramines and bromamines can be broadly classified as aliphatic, aromatic, and heterocyclic. Monohalo derivatives of primary amides, carbamates, and sulfonamides are sufficiently acidic to form metal salts. As with ammonia halamines, organo *N*-halamines disproportionate to *N,N*-dihalamines. *N*-Halamines can rearrange under the influence of heat, catalysts, or light, eg, *N*-chloroaniline rearranges to ring chlorinated anilines (66). *N*-Halamines are versatile reagents that react with a variety of substrates via radical and polar pathways. They add to olefins and acetylenes providing routes to cyclic compounds (67) and can also cleave certain C—C, C—N, and C—O bonds. They act as aminating, halogenating, dehydrohalogenating, and oxidizing agents and are useful in the preparation of many types of compounds (68–71).

Preparation. Substituted *N*-halamines are usually prepared by reaction of RR'NH with halogen, hypohalous acid, or hypohalite; where R is an organic substituent and R' is either an organic substituent or H.



They are generally produced in neutral to slightly acid solution. *N*-Halo-*N*-sodioamidates, *N*-halo-*N*-sodiocarbamiates, and *N*-halo-*N*-sodiosulfonamidates are exceptions, being prepared at moderately basic pH. *N*-Chloramines and *N*-bromamines are unstable to excess av Cl₂ or base, which can cleave the C—N bond forming potentially explosive compounds, eg, NCl₃ and NBr₃. In some cases the acid or base by-product must be neutralized as it is formed, since acid may prevent formation of halamine and base may cause decomposition. The reaction with halogen (eq. 4) is employed in commercial processes such as production of chloroisocyanurates; the base is added initially in the form of mono-, di-, or tri-sodium cyanurate. Other sources of electropositive halogen have also been used, eg, *N*-halamines (72), Cl₂O (73), *t*-C₄H₉OCl (74), *t*-C₄H₉OBr (75), and CH₃C(O)OBr (76). Sodium acetate has been used as an acid acceptor (77). In some cases, eg, in preparation of hexachloromelamine, an HCl acceptor may not be necessary if the reaction is carried out in dilute solution (78). *N*-Halocarbamiates and *N*-halosulfonamidates are formed directly by reaction of a carbamate or sulfonamide with hypohalite (79,80). Neutralization of the Na salts offers a convenient route to *N*-halocarbamates and *N*-halosulfonamides (79). In the preparation of a bromamine, a combination of Cl₂ or an *N*-chloramine and Br⁻ or Cl₂ plus Br₂ can be employed in order to eliminate the more expensive Br⁻ as a by-product: RR'NH + Cl₂ + Br⁻ + HO⁻ → RR'NBr + 2 Cl⁻ + H₂O (81,82). *N*-Bromo-*N*-chloramines can be prepared from equimolar quantities of the respective halamines: RNBr₂ + RNCl₂ → 2 RNBrCl (83).

ALIPHATIC COMPOUNDS

Amines. Although the chlorination of aqueous alkylamines is analogous to that of ammonia, mono- and dialkylamines generally chlorinate faster because of their higher basicities (13). Bromination rates are significantly faster than chlorination rates, and in some cases, eg, (CH₃)₂NH (*k* ~ 3 × 10⁹ M⁻¹s⁻¹ at 25°C), become diffusion rather than chemically controlled (21). Cleavage of the Si—N bond in trimethylsilylalkylamines by halogen in chloroform is a convenient route to primary and secondary *N*-haloalkylamines (84). Pure lower molecular weight *N,N*-dichloroalkylamines are volatile oils that are fairly stable at room temperature but unstable or explosive on heating. The stability of *N,N*-dibromamines is variable; tertiary compounds are more stable than secondary (85). Mixtures of *N,N*-dibromomethylamine [10218-83-4] and *N,N*-dichloromethylamine [7651-91-4], CH₃NCl₂, rapidly equilibrate under the influence of uv light to form *N*-bromo-*N*-chloromethylamine [76019-33-5] (86). *N,N*-Dichloramines are rapidly converted to *N,N*-dibromamines by reaction with Br⁻ in acetonitrile (87). *N*-Chloroalkylamines are useful for the preparation of substituted hydrazines by reaction with excess amine in the presence of base.

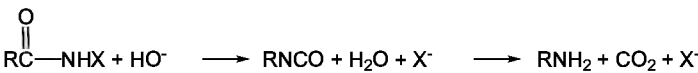


Uns-dimethylhydrazine is employed as a fuel in space applications. *N,N*-Dichloroalkylamines can be converted to nitriles in basic media or by treatment with CsF in acetonitrile (69).

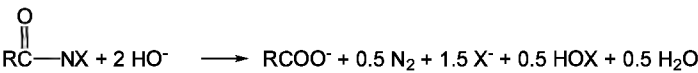


Protonated *N*-chloroalkylamines under the influence of heat or uv light rearrange to piperidines or pyrrolidines (Hofmann-Löffler reaction) (88). The free-radical addition of alkyl and dialkyl-*N*-chloramines to olefins and acetylenes yields β-chloroalkyl-, β-chloroalkenyl-, and δ-chloroalkenylamines (89). Various *N*-bromo- and *N*-chloropolyfluoroalkylamines have been synthesized whose addition products to olefinic double bonds can be photolyzed to fluoroazaalkenes (90).

Amides. Because amides are less basic, they chlorinate less rapidly than amines. *N*-Halamides are converted to amines in basic solution via intermediate formation of an isocyanate (Hofmann reaction) (91).

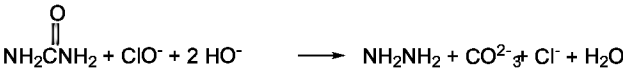


By contrast, base cleaves the C—N bond in *N,N*-dihalamides (92).



The Cr(II) catalyzed addition of *N*-bromamides and *N*-chloramides to olefins yields primarily *N*-(2-haloalkyl)amides which can be cyclized to oxazolines with alkoxide (93). *N*-Halamides are photochemically rearranged to 4-halamides which can be cyclized to γ-iminolactones and γ-lactones (75). *N*-Bromoacetamide [79-15-2], mp 102–105°C, is unstable to light and heat. Nevertheless, it is useful in organic synthesis as a brominating and oxidizing agent. It selectively oxidizes allylic alcohols and in the presence of HF and ether it reacts with olefins forming bromofluoro compounds and has been used in synthesis of steroids (94) and fluorosteroids (95).

Ureas. Chlorination of aqueous urea yields unstable *N*-chloro compounds. With excess ClO⁻ decomposition yields CO₂, N₂O, and NCl₃; the latter decomposes further to NO₃⁻ (96). Only two solid derivatives have been isolated: *N*-chlorourea [3135-74-8], mp 74–76°C, and *N,N'*-dichlorourea [2959-01-5], which decomposes at its mp of 83°C with evolution of NCl₃. As an amide, urea also undergoes the Hofmann reaction yielding hydrazine. This route to hydrazine was once employed commercially.

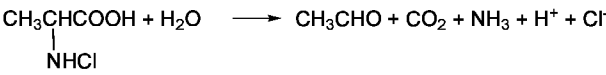


Various substituted *N*-bromo- and *N*-chloroureas have also been prepared (97). These compounds are useful for synthesis of oxazolidinones, and also hydrazine, hydrazo, and azo compounds. *N*-Bromourea [51918-81-1] is useful for selective oxidation of sugar derivatives (98).

Cyanamides and Derivatives *N*-Chloro-*t*-alkylcyanamides, RN(Cl)CN, are oils that have medicinal and other applications (99). Primary and secondary alkyl-*N*-chlorocyanamides add photochemically to olefins yielding 1:1 adducts. By contrast, *N*-chloro-*N'*-*t*-butylcyanamide initially rearranges photochemically to *N*-chloro-*N'*-*t*-butylcarbodiimide, (CH₃)₃CN=C=NCl, prior to addition to olefins giving carbodiimides (67,100).

N,N'-Dichlorocarbodiimide is useful in preparation of photothermographic materials (101). Chlorinated guanylurea (av Cl₂ 85° o), prepared from dicyanamide, is useful as a bleach for synthetic fabrics (102). Chlorazodin, dichloroazodicarbonamidine, NH₂C(=NCl) N=NC(=NCl) NH₂, [502-98-7] prepared from guanidine, is a pale yellow solid that is stable at room temperature but decomposes at 155°C (103). Once used as a surgical antiseptic, it finds use in vulcanization of rubber (104). *N*-Chloroamidines, eg, RNHC(CN)=NCl and CCl₂[C(NHR)=NCl]₂, exhibit fungicidal properties (105). *N*-Chloroamidines are useful for preparation of biocidal imidazoles (106) and thiadiazolines (107). *N*-Chloroguanidines, RNHC(=NCl)NHR', serve as starting materials for synthesis of imidazoles, oxadiazoles, and thiadiazoles (108,109).

Amino Acids. The formation of *N*-halo-α-amino acids involves halogenation of the acid anion (13). *N*-Chloro-α-amino acids decompose to aldehydes and nitriles, the selectivity depending on pH and stoichiometry (110). For example, *N*-chloroalanine decomposes in the 6.5–10 pH range.



In addition to aldehydes, nitriles are also formed either at lower pH (<5) or at higher pH by decomposition of *N,N*-dichloroalanine. When excess av Cl₂ is employed, the ammonia by-product is oxidized to nitrogen. The oxidation of amino acids by excess av Cl₂ is similar to breakpoint chlorination of ammonia but slower (26). *N*-Chloroamino acids are poorer disinfectants than ammonia chloramines (37). Glycine is useful as a stabilizer for av halogen in cooling towers, providing reduced corrosion (111). Esters of *N*-chloro- and *N,N*-dichloro-α-amino acids are stable and can be isolated in pure form. A large number of *N*-chloro- derivatives of α-aminobutyrate have been prepared and evaluated as disinfectants (11).

Carbamates. Lower alkyl *N*-halo- and *N,N*-dihalocarbamates are distillable liquids (70,112). *N*-Halo-*N*-metallocarbamates are crystalline hygroscopic solids. *N*-Chloro-*N*-sodiourethane [17510-52-0], C₂H₅OCONClNa, does not decompose on heating to 250°C (113), but violent decompositions have occurred at room temperature (114). *N*-Halocarbamates react with a variety of organic substrates, eg, the free-radical addition of *N*-chlorourethane [16844-21-6], C₂H₅OCONHCl, and *N,N*-dichlorourethane [13698-16-3], C₂H₅OCONCl₂, to olefins provides a convenient route to β-chlorocarbamates which can be converted to aziridines and alkylloxazolidones (93,115). *N*-Chloro-*N*-sodiourethane reacts with organoboranes forming *N*-alkylcarbamates (114), and with olefins, catalyzed by Os, forming vicinal hydroxy carbamates (116).

Sulfonamides. *N*-Halo-*N*-alkylsulfonamides, RSO₂NR'X, are relatively stable distillable liquids. Under the influence of uv light they form 1:1 adducts with olefins (67,100). *N*-*t*-Butyl derivatives rearrange forming precursors to cyclopropanes and sultams. *N*-Halo-*N*-sodioalkylsulfonamides, RSO₂NClNa, have been less extensively studied than their aromatic counterparts (70). The stability of these compounds approaches that of the aromatic sulfonamides (80). The dodecyl compound exhibits properties of both a disinfectant and a surfactant.

Other Aliphatic Compounds. Sodium *N*-chloro-*N*-alkylsulfamates have been patented as bleaching and disinfecting agents (117). *N,N*-Dichloro-1,8-diformamido-*p*-menthane [67700-31-6] can be used to prepare polyisocyanate-based resins (118). *N*-Bromo-*S,S*-dimethyl sulfoximine, (CH₃)₂S(O)NBr, undergoes nucleophilic substitution with phosphines and thioethers forming interesting salts (119). *N,N'*-Dibromo-*S,S*-dimethylsulfur diimide, (CH₃)₂S(NBr)₂, reacts similarly, also forming cyclic compounds (120). *N,N'*-Dichloro-*S,S*-dialkylsulfur diimides explode violently when heated. *O,O*-Diethyl *N,N*-dichlorophosphoramidate, (C₂H₅O)₂P(O)NCl₂, is a distillable oil that adds to olefins forming 1:1 adducts that can be reduced to *N*-(β-chloroalkyl)phosphoramidates (121). *N*-Bromotriphenyl-phosphine imine, (C H₅)₃P=NBr, (mp 170–172°C), is useful for synthesis of organically substituted compounds with PN≡P, PN≡S, and PN≡As linkages (122). *N*-Chloro-(bis-trimethylsilyl)amine [4148-01-0], [(CH₃)₃Si]₂NCl, a yellow liquid (bp 149°C), reacts with NaN₃ forming a tetrazadiene and with BCl₃ to give hexachloroborazene (123).

AROMATIC COMPOUNDS

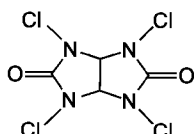
Sulfonamides. Chloramine-T, *N*-chloro-*N*-sodiummethylbenzenesulfonamidate trihydrate [127-65-1], CH₃C H₄SO₂NClNa 3H₂O, a white to slightly yellow solid, effloresces in air losing chlorine, becoming less soluble in water (71). It has a mp of 175°C, an av Cl₂ of 25° o, and is moderately soluble in cold water giving pH ~9. Heating above 130°C may lead to explosion. The anhydrous product may explode at lower temperatures. Chloramine-T can be prepared by reaction of the amide with NaOCl. It was originally introduced in 1916 as a germicide. Mustard gas, (ClC₂H₄)₂S, is rendered ineffective by oxidation with chloramine-T (71). Chloramine-T is used in analysis and organic synthesis (70,71). Bromine analogues are also known, ie, bromamine-T [41085-71-6] and *N,N*-bromo-*N*-sodio-4-nitrobenzenesulfonamidate [41085-73-8]. The bromo derivatives are also used in organic synthesis (70). Chloramine-B, *N*-chlor-*N*-sodiobenzenesulfonamidate [127-52-6], is prepared similarly to chloramine-T. It has been used as a disinfectant in dairies (124). A bromine equivalent, bromamine-B [16917-09-2], has also been prepared. The chloro and bromo compounds are used in analytical chemistry and in organic synthesis. Polymer-bound *N*-chloro-*N*-sodiobenzenesulfonamidate, prepared via functionalization of poly(styrene-*m*-divinylbenzene), is useful in water disinfection (125).

Sulfonamides. Dichloramine-T, *N,N*-dichloro-4-methylbenzenesulfonamide [473-34-7], CH₃C H₄SO₂NCl₂, mp 80°C, can be prepared by chlorination of the free amine or chloramine-T. It is also formed via disproportionation of chloramine-T (126). It is almost insoluble in water and has been used as a topical dressing and an antivesicant ointment (127). It is also used in organic synthesis. Dichloramine-B, *N,N*-dichlorobenzenesulfonamide [473-29-0], C H₅SO₂NCl₂, has been used as a deodorant and bleach for certain oils. Bromine analogues, ie, dibromamine-B [938-05-6], dibromamine-T [21849-4-1], and bromochloramine-T [27824-67-5], have also been prepared. Halazone, *p*-(*N,N*-dichlorosulfamoyl)benzoic acid [80-13-7], HOCC H₄SO₂NCl₂, is a white solid which decomposes at ~195°C and is slightly soluble in water. It was used for emergency disinfection of water prior to, during, and after World War II (128). The homologue 3-(dichlorosulfamoyl)phthalic acid [67700-34-9], (HOOC)₂C H₃SO₂NCl₂, is also a useful disinfectant (129).

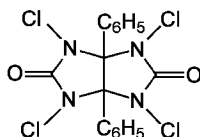
Other Aromatic Compounds. *N*-Chloro-*N*-substituted-*p*-nitroanilides, and other compounds, serve as sources of hypochlorite when mixed with alkaline materials (130). *N*-Chlorophenyldiguanidino compounds were once used as laundry bleaches (131,132). Sodium *N*-chloro-*N*-arylsulfamates have been patented as bleaches and disinfectants (118). *N*-Halophthalimides and *N*-haloquinolimides are converted under alkaline conditions to isatoic and 3-azaisatoic anhydrides, respectively, which are useful in production of pharmaceuticals and agrochemicals (133). *N*-Bromo derivatives of amides, imides, and sulfonamides are prepared in near quantitative yield using CH₃C(O)OBr (76). *N*-Bromophthalimide [2439-85-2] and *N*-bromosaccharin [35812-01-2], a derivative of *o*-sulfamoylbenzoic acid, are useful brominating agents in analytical chemistry (134). Numerous *N*-halo derivatives of aromatically substituted amines, such as ureas, cyanamides, carbamates, and amino acids, have also been prepared.

HETEROCYCLIC COMPOUNDS

Glycolurils. Chlorinated glycolurils were developed in the 1950s to 1960s for protection against chemical agents and as bleaches, disinfectants, and foliage protectants (135–138). The most important is 2,4,6,8-tetrachloro-2,4,6,8-tetrazobicyclo(3.3.0)octane-3,7-dione [776-19-2] (2). The parent compound, glycoluril, is readily prepared by condensation of urea and glyoxal. Substituted glycolurils are prepared by reaction of urea with the appropriate diketone (139). Like the chlorinated hydantoins, the chlorinated glycolurils are sparingly soluble in water. Tetrachloroglycoluril, eg, has a solubility of 77 ppm at 25°C. Although it has a theoretical av Cl₂ of 101.6° o, only 10–20° o titrates as FAC. It was once used in swimming pool disinfection. It has been employed in wastewater disinfection as a component of Ca(OCl)₂ tablets called Sanuril (140). 1,3,4,6-Tetrachloro-3α,6α-diphenylglycoluril [51592-06-4] (3), Iodogen, is useful as a disinfectant (141) and is widely used in radioimmunoassay as an oxidizing agent for preparation of ¹²⁵I labeled proteins, glycoproteins, and peptides (142). Bromo and bromochloro analogues have also been prepared (81,132,135).



(2)

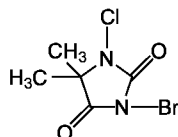


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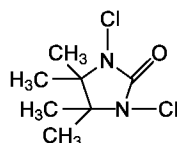
Hydantoins. Chlorinated hydantoins, first introduced in the 1930s, did not find wide use because of low dissolution rate. An additional disadvantage was the fact that hydrolysis of the second chlorine required a temperature of $\sim 70^\circ\text{C}$. 1,3-Dichloro-5,5-dimethylhydantoin [118-52-5] (DCDMH, Halane) (1) (143) was once used as a chemical warfare decontaminating agent (144). It has been used as a chlorinating agent, disinfectant, industrial deodorant, and as a laundry bleach. It is no longer used in home laundering because of changing needs of synthetic fabrics but is used to a small extent in commercial laundries where temperatures of $\sim 70^\circ\text{C}$ can be used. At pH 9 it decomposes to $(\text{CH}_3)_2\text{CHNCl}$, Cl^- , N_2 , and CO_2 (145).

1-Bromo-3-chloro-5,5-dimethylhydantoin [16079-88-2] (BCDMH) (4) (81,83,132,146) is used in industrial water treatment and in sanitizing spas and hot tubs. Its use in outdoor swimming pools is limited because of cost, a very slow dissolution rate, and the fact that bromine is not stabilized against photolytic decomposition by dimethylhydantoin. The bactericidal properties of BCDMH have been studied in detail (147). The bromine hydrolyzes to a greater extent than the chlorine. Since excess bromide is normally present, it reacts rapidly with any HOCl or ClO^- formed by hydrolysis of BCDMH to generate Br_2 , eg, $\text{HOCl} + \text{Br}^- \rightarrow \text{HOBr} + \text{Cl}^-$, $k = 2.95 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$ at 25°C . Typical commercial products are based on BCDMH. However, one product is a mixture of DCDMH, BCDMH, and 1,3-dichloro-5-ethyl-5-methylhydantoin [89415-87-2] (148). BCDMH is also useful in control of biofouling in water recirculating systems (149), in toilet bowl cleaning (150), in metal recovery (151), and in laundry bleaching (152).

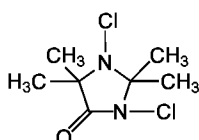
1,3-Dibromo-5,5-dimethylhydantoin [77-48-5] (81,82,143) is employed in organic synthesis (153–156).



(4)



(5)

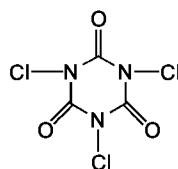


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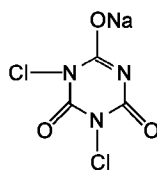
Imidazolidinones. Several mono and dichloro isomers have been prepared and tested as disinfectants (157):

1-chloro-4,4,5,5-tetramethylimidazolidin-2-one [58816-19-6]; 1,3-dichloro-4,4,5,5-tetramethylimidazolidin-2-one [58816-20-9] (5), mp $102\text{--}104^\circ\text{C}$; 1-chloro-2,2,5,5-tetramethylimidazolidin-4-one [38951-95-8], mp $157\text{--}158^\circ\text{C}$; and 1,3-dichloro-2,2,5,5-tetramethylimidazolidin-4-one [128780-87-0] (6), mp $69\text{--}71^\circ\text{C}$ (158). In water, these compounds are somewhat less stable but better disinfectants than the oxazolidinones. They have potential for water disinfection and in hard surface cleaners. 1-Bromo-3-chloro- [108602-19-3], mp $102\text{--}104^\circ\text{C}$, and 1,3-dibromo- [108602-18-2], mp $119\text{--}121^\circ\text{C}$, derivatives of 4,4,5,5-tetramethylimidazolidin-2-one have been prepared.

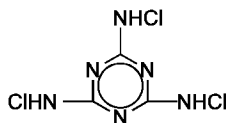
Isocyanurates. Chlorination of cyanuric acid in the presence of base produces dichloroisocyanuric acid (DCCA, HCl_2Cy , where $\text{Cy} =$ isocyanurate anion), ie, 1,3-dichloro-*s*-triazine-2,4,6-(1*H*, 3*H*, 5*H*)-trione [2782-57-2] and trichloroisocyanuric acid (TCCA, Cl_3Cy), ie, 1,3,5-trichloro-*s*-triazine-2,4,6-(1*H*, 3*H*, 5*H*)-trione [87-90-1] (7). DCCA forms various simple salts, eg, potassium dichloroisocyanurate [2244-21-5] KCl_2Cy , sodium dichloroisocyanurate [2893-78-9] (SDCC), $\text{Na}\cdot\text{Cl}_2\text{Cy}$, (8), and its mono [52671-45-1], $\text{NaCl}_2\text{Cy}\cdot\text{H}_2\text{O}$, and dihydrates [51580-86-0], $\text{NaCl}_2\text{Cy}\cdot 2\text{H}_2\text{O}$. A number of double salts have also been prepared, eg, $\text{Cl}_3\text{Cy}\cdot\text{KCl}_2\text{Cy}$ [30622-37-8] and $\text{Cl}_3\text{Cy}\cdot 4\text{KCl}_2\text{Cy}$ [30622-37-8]. Some properties of chloroisocyanurates have been given (12) (see CYANURIC AND ISOCYANURIC ACIDS). Bromine and bromochloro derivatives of isocyanuric acid (81) include HBrClCy [89325-49-5], HBr_2Cy [15114-43-9] (72), NaBrClCy [20367-88-8], NaBr_2Cy [15114-34-8], BrCl_2Cy [89696-38-8], Br_2ClCy , and Br_3Cy [17497-85-7] (72). Because of hydrolysis, the tribromo compound can only be prepared in nonaqueous media.



(7)



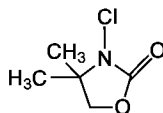
(8)



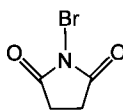
(9)

Melamines. Hexachloromelamine [2428-04-8] has a theoretical av Cl_2 of 128% (78,159). It is less stable than the trichloro compound: N^2,N^4,N^6 -trichloro-2,4,6-triamino-1,3,5-triazine [12379-38-3] (9), av Cl_2 ~93%, mp 175°C, slightly soluble in water. Several bromo analogues have been prepared (82,159).

Oxazolidinones. 3-Chloro-4,4-dimethyl-2-oxazolidinone [58629-01-9] (10) has been extensively evaluated as a disinfectant (157). It is prepared by phosgenation of $(\text{CH}_3)_2\text{CH}(\text{NH}_2)\text{CH}_2\text{OH}$ followed by chlorination in the presence of caustic. It is a white crystalline solid with a theoretical av Cl_2 of 48.1%, a mp of 71–72.5°C, and a solubility of 1.2% in H_2O . It hydrolyzes to only a very slight extent and consequently is very stable in aqueous media relative to other chlorine-based disinfectants. However, disinfection effectiveness is significantly lower than with hypochlorite or chloroisocyanurate. Nevertheless, it may find use in applications where kill time is not of primary importance, eg, cooling towers. A number of bromine analogues have also been prepared, eg, 3-bromo-4,4-dimethyl-2-oxazolidinone [60491-95-4] is an orange solid with mp 118–120°C. Because of greater hydrolysis it is less stable in water than the chloro derivative but is a better disinfectant.



(10)



(11)

Succinimides. *N*-Chlorosuccinimide, 1-chloropyrrolidine-2,5-dione [128-09-6], is a white solid with a slight chlorine odor, a mp of 150–151°C, and a solubility in water of 1.4% at 25°C. It is used in organic synthesis for highly selective oxidation of primary and secondary alcohols to carbonyl compounds, providing improved synthesis of prostaglandins (160), and in conversion of allylic and benzylic alcohols to halides (161). It selectively cleaves tryptophanyl peptide bonds (162) and is useful in fluorometric analysis of proline and hydroxyproline (163). *N*-Bromosuccinimide, [128-08-5] (NBS) (11) is a solid with mp of 173–175°C and solubility of 1.4% at 25°C. It is especially useful in organic synthesis for allylic bromination (Wohl-Ziegler reaction) (164), aromatic ring (165) and side-chain bromination, for oxidation, eg, alcohols to carbonyl compounds, for dehydrohalogenation (68), and is used in the commercial production of cortisone (166) and vitamin D₃.

Other Heterocyclic Compounds. 1,3-Dichlorotetrahydroquinazoline-2,4-dione [23767-45-5] is useful as a laundry bleach. 2-Chloro-4-thiazolines are useful reagents for organic synthesis (167). *N*-Chloropiperidines, *N*-chloropiperidones, and 1,4-dichloro-2,2,5,5-tetrasubstituted-piperazine-3,6-diones have been evaluated as disinfectants (168). 1,3,5-Trichloro-2,4-dioxohexahydrotriazine [67700-33-8] is a useful bactericide (169). *N*-Chloro-2-substituted-imidazoles have been prepared for impregnating clothing for protection against chemical agents such as mustard gas (170). 1-Chlorobenzotriazole [21050-95-3] is useful in organic synthesis for oxidation of alcohols to carbonyl compounds and hydrazo compounds to azo compounds (171). 1,3-Dihalouracils have utility as pesticides, fungicides, bleaching, and sanitizing agents (172). The cyclic amide, *N*-bromo-ε-caprolactam [2439-83-0], mp 64–66°C, functions as an allylic brominating agent similar to *N*-bromosuccinimide but does not require activation (173). *N*-Chloro- and *N*-bromopolymaleimides are useful as halogenating agents (174).

Analysis

The available halogen in *N*-halamines is determined by reaction with excess iodide in acid media followed by titration with standard thiosulfate. For mixed bromochloro *N*-halamines, the ratio of av Br_2 to av Cl_2 can be determined by reduction followed by potentiometric titration of Br^- and Cl^- . Standard ir spectra are useful for identification of *N*-halamines (175). A number of instrumental, titrimetric, and colorimetric methods are available for determining various forms of chlorine in dilute aqueous solution, ie, total, free, combined, mono-, di-, and trichloramine (176). Test kits typically based on the Palin or DPD method, employing manual color comparators or spectrophotometers, are available for routine analysis in the laboratory or in the field (177). Hypochlorous acid can be determined directly by sweep voltammetry (178) and amperometry using a membrane electrode (179). Because they undergo hydrolysis to HOCl , inorganic and organic chloramines can interfere with instrumental and colorimetric FAC measurements (180). The DPD method is also applicable to determination of free and combined av Br_2 (181). Mono-, di-, and trichloramine can also be quantitated by extraction of dilute aqueous solutions with CCl_4 followed by uv spectrophotometry (182). Gc can also be used to determine NCl_3 in aqueous solution after extraction with CCl_4 . Trichloramine can be determined in the gas phase by uv or gas chromatography (gc).

Economic Aspects

The estimated 1990 worldwide consumption of monochloramine for hydrazine manufacture was 55,000 t. Consumption data on use of monochloramine in water treatment are not available. The U.S. consumption of chloroisocyanurates and halogenated hydantoin in 1986 was 44,045 and 3,409 t, respectively (183). Consumption of tetrachloroglycoluril and other specialty *N*-halamines, eg, trichloromelamine, is small.

Uses

Monochloramine is used in water treatment and as an intermediate in the manufacture of hydrazine (qv). Chloroisocyanurates are employed primarily for sanitation in swimming pools and spas. They are also used in hard surface cleaners, laundry products, as toilet bowl cleaners, eg, TCCA and SDCC NaBr, and as shrink-proofing agents in wool finishing. Whereas TCCA is the principal product in pool and spa use, SDCC is the main product in nonpool spa applications. Dichlorodimethylhydantoin is employed as a bleaching agent in industrial and institutional cleaning products (see BLEACHING AGENTS). Bromochlorodimethylhydantoin is used primarily as a sanitizer in spas and to a smaller extent in swimming pools. Industrial water treatment applications include cooling towers, air washers, pasteurizers, and paper mills (see WATER, INDUSTRIAL WATER TREATMENT). Small amounts of bromochlorodimethylhydantoin and tetrachloroglycoluril are used as components of Ca(OCl)₂ tablets called Sanuril that are employed in wastewater treatment. N-Chlorodimethyloxazolidinone, formed *in situ* from av Cl₂ and dimethyloxazolidinone is employed as an algistat in cooling towers and swimming pools. Trichloromelamine is employed as a disinfectant, eg, in restaurants (see DISINFECTANTS AND ANTISEPTICS). N-Halamines such as N-bromo- and N-chlorosuccinimide, N-bromocaprolactam, N,N-dibromo- and N,N-dichlorodimethylhydantoin, chloramine-T, N,N-dichlorourethane, dibromo- and trichloroisocyanuric acids, etc are employed as selective reagents for halogenation, oxidation, and other transformations in research, in analysis, and in small-scale production of specialty chemicals, pharmaceuticals, flavors, fragrances, etc.

Safety, Handling, and Toxicity

Chloramines and bromamines react with moisture releasing potentially corrosive, toxic, and explosive gases and should be stored under dry conditions at moderate temperatures, segregated from incompatible materials. Since they are highly reactive they should not be mixed with other materials such as acids, bases, reducing agents, oxidizing agents, organic compounds, ammonium compounds, etc, since vigorous reactions can occur, accompanied by fire and even explosions, liberating large amounts of heat and potentially toxic gases. N-Halamines are irritating to the skin, eyes, and mucous membranes. However, they are nonirritating under use conditions in dilute aqueous solution. Acute oral toxicities, LD₅₀ (mg kg, rat) are TCCA 490, SDCC 735, and BCDMH 600 (184). Residual cyanuric acid from use of chloroisocyanurates has low toxicity. Monochloramine has been shown to be a weak mutagen and its use in drinking water is under review by the EPA (33,185).

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CHLORAMPHENICOL.

See ANTIBIOTICS, CHLORAMPHENICOL.

CHLORINATED BIPHENYLS.

See BIPHENYL AND TERPHENYLS; CHLOROCARBONS AND CHLOROHYDROCARBONS, TOXIC AROMATICS.

CHLORINE.

See ALKALI AND CHLORINE PRODUCTS.

CHLORINE OXYGEN ACIDS AND SALTS

Dichlorine monoxide, hypochlorous acid, and hypochlorites,
Chlorous acid, chlorites, and chlorine dioxide,
Chloric acid and chlorates,

DICHLORINE MONOXIDE, HYPOCHLOROUS ACID, AND HYPOCHLORITES

Oxidation States

Chlorine has formal positive oxidation numbers (states) in oxychlorine compounds since its appreciable electronegativity (2.83) on the Allred-Rochow scale is exceeded by that of oxygen (1). References to positive chlorine in this article are strictly in the formal sense unless stated otherwise. All chlorine compounds are strong oxidants because the transfer of electrons to the orbitals of electronegative chlorine is favored in reactions with compounds of less electronegative elements. Chlorine oxides and oxo-acids exhibit the lack of stability expected of compounds having bonds between two strongly electronegative elements. The decomposition reactions of these compounds are, therefore, always energetic and violent in many cases (Table 1). The chemical properties of chlorine oxides and oxo-acids display a trend toward greater thermodynamic and kinetic stability with increasing oxidation state. It is possible to isolate pure perchloric acid and its anhydride, Cl₂O₇, whereas pure hypochlorous, chlorous, and chloric acids have not been obtained. The reduction potentials of the oxo-acids exhibit a similar trend in that the strongest oxidants have chlorine in its lower states of oxidation. Compounds of chlorine having intermediate oxidation states exhibit a strong tendency to disproportionate.

Table 1. Chlorine Oxides^a and Oxo-Acids

Formula	CAS Registry Number	Oxidation state	Stability
<i>Oxides</i>			
Cl ₂ O	[7791-21-1]	+1	anhydride of HOCl; yellowish brown gas at 25°C; explodes when heated or sparked
Cl ₂ O ₂	[12292-23-8]	+2	<i>t</i> _{1/2} of gas 4.8 d at 78°C
Cl ₂ O ₃	[17496-59-2]	+3	anhydride of HClO ₂ ; explodes below 0°C
ClO ₂	[10049-04-4]	+4	odd electron molecule; yellow gas; explodes at >6.7 kPa ^b
Cl ₂ O ₄	[27218-16-2]	+1, +7	pale yellow liquid; decomposes to Cl ₂ , O ₂ , and Cl ₂ O
Cl ₂ O	[12442-63-6]	+6	red liquid; gas decomposes to Cl ₂ O ₄ + O ₂
Cl ₂ O ₇	[12015-53-1]	+7	anhydride of HClO ₄ ; colorless liquid; can be distilled under reduced pressure
<i>Acids</i>			
HOCl ^c	[7790-92-3]	+1	very weak acid, p <i>K</i> _a 7.54; cannot be concentrated
HClO ₂	[13898-47-0]	+3	decomposes rapidly at 25°; p <i>K</i> _a ~2.0; cannot be concentrated
HClO ₃	[7790-93-4]	+5	decomposes slowly at ~40% and 25°C; cannot be concentrated
HClO ₄	[7601-90-3]	+7	can be concentrated

^a Anhydride of chloric acid, Cl₂O₅, is unknown. Oxides with even number of oxygen atoms are mixed anhydrides. Other chlorine oxides such as the radicals ClO, ClO₃, and ClO₄ are known. Chlorine monoxide [14989-30-1], ClO, plays a key role in depletion of the ozone layer.

^b To convert kPa to mm Hg, multiply by 7.5.

^c The isomeric HClO is an unstable compound formed in the earth's ozone layer.

The oxo-anions of chlorine are weaker oxidants than the corresponding acids. Because they are also more stable, it is not too difficult to isolate certain salts of those acids that can be obtained only in aqueous solution. Hypochlorites and chlorites are hydrolyzed in aqueous solution since HOCl and HClO₂ have acid dissociation constants of ~10⁻⁸ and 10⁻², respectively; however, aqueous chloric and perchloric acids are fully ionized.

The chlorine oxides are anhydrides or mixed anhydrides of the chlorine oxo-acids; oxides with an odd number of oxygens are simple anhydrides whereas those with an even number are mixed anhydrides.

Chlorine in dichlorine monoxide, hypochlorous acid, and ionic hypochlorites is in the +1 formal oxidation state. Other compounds where univalent chlorine is bonded to oxygen are the alkyl, aryl, and acyl hypochlorites and other unipositive chlorine compounds such as ClOSF₅, ClOSO₂F, ClONO, ClONO₂, and ClOClO₃. The latter compounds are chlorine derivatives of the corresponding acids and can also be considered as mixed anhydrides of HOCl and the corresponding acid. The polar bonding in these compounds imparts a partial positive charge on the first chlorine atom. Along with HCl, ClONO₂ forms a chlorine reservoir in the upper stratosphere that plays an important role in depletion of the ozone layer.

DICHLORINE MONOXIDE

Dichlorine monoxide is the anhydride of hypochlorous acid; the two nonpolar compounds are readily interconvertible in the gas or aqueous phases via the equilibrium: Cl₂O + H₂O⇌2HOCl. Like other chlorine oxides, Cl₂O has an endothermic heat of formation and is thus thermodynamically unstable with respect to decomposition into chlorine and oxygen. Dichlorine monoxide typifies the chlorine oxides as a highly reactive and explosive compound with strong oxidizing properties. Nevertheless, it can be handled safely with proper precautions.

Physical Properties

At ordinary temperatures dichlorine monoxide is a brownish yellow gas resembling bromine. For the condensed red-brown liquid the vapor pressure over the range 173–288 K is given by: log *p* (kPa) = 6.995 – 1373 / *T* [log *p* (mm Hg) = 7.87 – 1373 / *T*] (2). Its bp, 2.0°C, and Δ*H*_{vap}, 25.9 kJ / mol (6.2 kcal / mol), are calculated from vapor pressure data. The mp of Cl₂O is –120.6°C (3). It readily dissolves in water to give a solution of hypochlorous acid containing a small equilibrium amount of Cl₂O. At –9.4°C the saturation solubility is 143.6 g Cl₂O / 100 g of H₂O, which is equivalent to 71% HOCl. Henry's constant, using molarity in place of mol fraction, for the vapor–liquid equilibrium at 3.46°C is *K* = [Cl₂O]_g / [Cl₂O]_{aq} = 14.23 kPa / (*M*) [106.7 mm Hg / (*M*)] (4). Thermodynamic properties of gaseous Cl₂O are Δ*H*^o of solution, 36.6 kJ / mol (8.74 kcal / mol); Δ*H*_f^o, 87.9 kJ / mol (21.0 kcal / mol); Δ*G*_f^o, 105.1 kJ / mol (25.1 kcal / mol); *S*^o, 268.0 J / (molK); [64.1 cal / (molK)]; and *C*_p, 47.8 J / (molK) [11.4 cal / (molK)] (5). Microwave spectroscopic measurements show Cl₂O to be a

nonlinear molecule with C_{2v} symmetry (6,7). The uv spectrum shows a maximum near 260 nm. Molar absorptivities of 610 cm⁻¹ (8) and 511 cm⁻¹ (9) are reported. The ir spectrum shows three fundamental bands at ca 296, 631, and 671 cm⁻¹ (10).

Chemical Properties

Explosion of gaseous dichlorine monoxide can be initiated by spark or heat. The liquid is shock sensitive but less so than ClO₂ (11). The minimum explosive concentration of gaseous Cl₂O in oxygen at 23°C and 101 kPa (1 atm) in faint daylight is 23.5 mol % (12). Explosions are mild in the 25–30° range but become progressively more violent at higher concentrations. The effect of various diluent gases on the explosion limit at various total pressures has been determined in the complete absence of light. The extrapolated explosion limit in O₂ is ~33 mol % (13). The threshold for spark initiated decomposition of pure Cl₂O is 0.53 kPa (4.0 mm Hg). Dichlorine monoxide decomposes thermally and photochemically into Cl₂ and O₂. The photolytic decomposition, initiated by cleavage into ClO, O, and Cl free radicals, is sensitized by Cl₂ (14). Significant concentrations of ClO₂ are generated from Cl₂O by controlled thermal decomposition or irradiation of CCl₄ solutions. Photolysis of matrix-isolated Cl₂O yields ClClO, (ClO)₂, and ClO (15). Gaseous Cl₂O decomposes thermally in 12–24 h at 60–100°C, but at 150°C the reaction is complete in only a few minutes; above 110°C the reactions terminate in explosion (16). The decomposition is preceded by an induction period inversely proportional to the starting Cl₂O concentration. Several mechanisms, some involving chains, have been proposed for this heterogeneous reaction (17,18).

Dichlorine monoxide reacts with a variety of inorganic substances, eg, its reaction with N₂O₅ is a convenient route to ClNO₃ (19). The latter is also formed from other nitrogen oxides. The stoichiometry depends on the reaction phase, and the key step appears to be ClO + NO₂ → ClNO₃ (20). Chlorine dioxide is an intermediate in certain reactions of Cl₂O as in the preparation of chloryl fluoride and in the formation of ionic complexes from SO₃ and AsF₅ (21,22). The transformation of metal halides into oxy-halides by Cl₂O apparently involves hypochlorite intermediates (23). Some reactions of Cl₂O with inorganic compounds are summarized in Table 2. Dichlorine monoxide can be used for generation of singlet oxygen in the chemical oxygen iodine laser (COIL) (30).

Table 2. Reactions of Cl₂O With Inorganic Compounds

Reaction	Reference
$\text{Cl}_2\text{O} + 3 \text{F}_2 \xrightarrow[\text{CaF}_2]{78^\circ\text{C}} \text{ClF}_3\text{O} + \text{ClF}_3$ >80%	24
$2 \text{Cl}_2\text{O} + \text{AgF}_2 \xrightarrow{65-70^\circ\text{C}} \text{ClO}_2\text{F} + \text{AgF} + \frac{3}{2} \text{Cl}_2$	25
$5 \text{Cl}_2\text{O} + 3 \text{AsF}_5 \xrightarrow{-78 \text{ to } 50^\circ\text{C}} 2 \text{ClO}_2\text{AsF}_6 + \text{AsOF}_3 + 4 \text{Cl}_2$	21
$\text{Cl}_2\text{O} + \text{N}_2\text{O}_5 \xrightarrow{0^\circ\text{C}} 2 \text{ClNO}_3$ 90%	19
$4 \text{Cl}_2 + 3 \text{SO}_3 \xrightarrow[\text{CFCl}_3]{27^\circ\text{C}} (\text{ClO}) (\text{ClO}_2) [\text{S}_3\text{O}_{10}] + 3 \text{Cl}_2$	22
$\text{Cl}_2\text{O} + \text{TiBr}_4 \rightarrow \text{TiOBr}_2 + \text{Br}_2 + \text{Cl}_2^a$	27
$3 \text{Cl}_2\text{O} + 2 \text{BCl}_3 \xrightarrow{-78^\circ\text{C}} \text{B}_2\text{O}_3 + 6 \text{Cl}_2^b$	28
$2 \text{Cl}_2\text{O} + \text{P}(\text{NCl}_2)_3 \rightarrow \text{PO}_2\text{Cl} + 3 \text{NCl}_3$	29

^a Similar reactions occur with TiCl₄, SnBr₄, SnCl₄, and PbCl₄ (23,26).

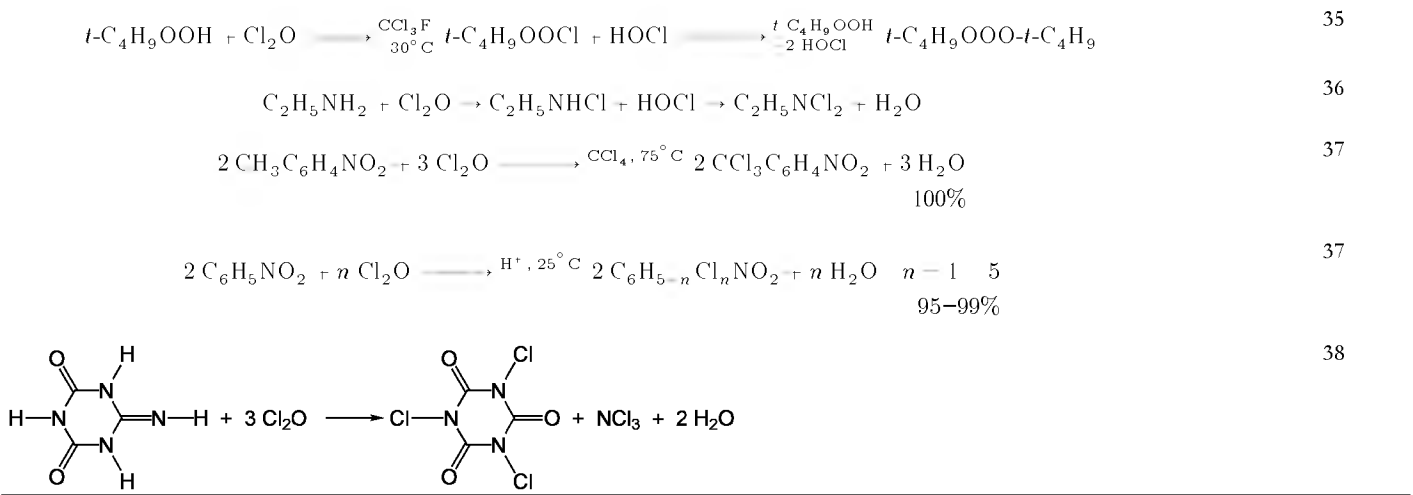
^b AlBr₃ similarly gives Al₂O₃, but with AlCl₃ there is no reaction.

Dichlorine monoxide, which exists in very low equilibrium concentrations in dilute HOCl solutions, is nevertheless a kinetically significant reactant. For example, although tetracyanonickelate(II) can be oxidized by chlorine in aqueous solution to *trans*-Ni(III) (CN)₄(H₂O)₂ ;, the second-order rate constant at 25°C for oxidation with Cl₂O is 40 times greater than for Cl₂ and 2.6 × 10⁷ greater than for HOCl (31).

The organic chemistry of Cl₂O has not been extensively explored. Some representative reactions are shown in Table 3. The liquid-phase reaction of Cl₂O with alkanes exhibits the following overall stoichiometry: 2 RH + Cl₂O → 2 RCl + H₂O. The photoinduced reaction proceeds by a free-radical chain mechanism, giving a mixture of chlorination products (32). In contrast, the dark reaction results in high selectivity for tertiary chlorination (39). The proposed mechanism for the reaction of Cl₂O with cyclohexene involves direct addition to the olefin, forming the intermediate *trans*-2-chlorocyclohexyl hypochlorite, and a simultaneous homolysis of Cl₂O to produce a number of products, eg, the chlorohydrin and 2-chlorocyclohexene, arising from radical and ionic pathways (33). Dichlorine monoxide reacts with COF₂ in the presence of CsF to give CF₃OCl (40). In contrast, F₂O produces CF₃OOOCF₃ via the intermediate CF₃OOF, illustrating the reversal of polarity of the halogen–oxygen bond in the case of the more electronegative fluorine (41).

Table 3. Reaction of Cl₂O With Organic Compounds

Reaction	Reference
$\text{C}_3\text{H}_7\text{Cl} \xrightarrow[\text{CCl}_4, \text{ } h\nu]{\text{Cl}_2\text{O}} \text{CH}_3\text{CH}_2\text{CHCl}_2 + \text{CH}_3\text{CHClCH}_2\text{Cl} + \text{ClCH}_2\text{CH}_2\text{CH}_2\text{Cl}$ 43% 42% 15%	32
$\text{CCl}_2=\text{CHCl} \xrightarrow{\text{CCl}_4}{\text{Cl}_2\text{O}} \text{CCl}_3\text{CHCl}_2 + \text{CCl}_3\text{CHO} + (\text{CCl}_3\text{CHCl})_2\text{O}$	33
$\text{C}_6\text{H}_5\text{OH} \xrightarrow{\text{CCl}_4}{\text{Cl}_2\text{O}} o\text{-ClC}_6\text{H}_4\text{OH} + p\text{-ClC}_6\text{H}_4\text{OH}$ 22% 65%	34

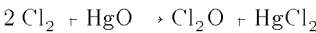


Dichlorine monoxide is a powerful and selective reagent for either side-chain or ring chlorination of deactivated aromatic substrates providing excellent yields under mild conditions where conventional reagents fail or require harsh conditions (37,42). The strong electrophilicity of Cl₂O was further demonstrated in studies using *p*-xylene as the substrate. The specific reactivity of Cl₂O was equivalent to Cl₂ and 2.2 × 10³ greater than that of Br₂. By contrast, the reactivity of HOCl was insignificant (43,44). Kinetic studies have shown that Cl₂O is a probable intermediate in the chlorination of anisole by HOCl (45). Dichlorine monoxide has also been postulated as an intermediate in the addition of HOCl to olefins (46,47).

Dichlorine monoxide, generated *in situ* in the presence of CCl₄ by reaction of CO₂ and NaOCl, has been used in preparation of substituted hydrazines (48). Dichlorine monoxide reacts with finely divided cyanuric acid in a fluidized bed forming dichloro- and trichloroisocyanuric acids (49) and with sodium cyanurate monohydrate yielding sodium dichloroisocyanurate monohydrate (50) (see CYANURIC AND ISOCYANURIC ACIDS).

Preparation

On a laboratory scale, gaseous dichlorine monoxide is conveniently generated by reaction of chlorine gas with mercuric oxide in a packed tubular reactor. High yields are favored by cooling the reactor, using pure chlorine diluted with an inert gas, eg, air or N₂, and mixing dry HgO with an inert material, eg, sand, pumice, kieselguhr, crushed brick, crushed glass tubing, or saddles (51–53). Use of excess HgO ensures complete conversion of chlorine thus eliminating contamination of the Cl₂O. The spent HgO can be regenerated by treatment with aqueous caustic, filtering, washing with water, and drying at 110°C. If liquid Cl₂O is desired, the exit gases can be passed through a trap cooled with dry ice and alcohol, acetone, or chloroform (3). In the static reaction of Cl₂ with HgO at –78°C, high yields of Cl₂O are obtained, and with excess Cl₂ the reaction is (54)



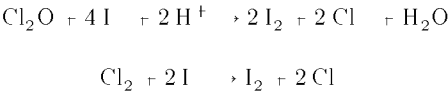
A solution of Cl₂O can be prepared by addition of HgO to a solution of Cl₂ in CCl₄ followed by filtration to remove the basic mercuric chloride. A dilute solution containing a few percent Cl₂O is obtained in 90% yield and is stable when stored in the dark under refrigeration. Moist soda ash can be used in place of HgO but the yield is reduced to about 40% (51).

Dichlorine monoxide can also be prepared from concentrated HOCl solutions by vacuum distillation (55), by stripping with air (56,57), and by treatment with anhydrous Ca(NO₃)₂ (58). It can also be prepared by treatment of aqueous HOCl or Ca(OCl)₂, mixed with (C₄H₉O)₃PO₄ and CCl₄, with concentrated sulfuric acid (59,60).

Routes more amenable to commercial-scale production are based on reaction of chlorine with sodium bicarbonate, carbonate, or sesquicarbonate. For example, reaction of Cl₂ and water vapor with soda ash in a countercurrent tower reactor give Cl₂O mixed with Cl₂, HOCl, H₂O, and CO₂ (61). The reaction can also be carried out in a fluidized-bed reactor employing sodium sesquicarbonate (62). High yields of Cl₂O are reported for the reaction of Cl₂, diluted with moist air, with porous soda ash (63). A continuous scheme for generating Cl₂O involves reaction of Cl₂ with anhydrous soda ash in a fixed or fluidized-bed reactor at 180°C (64). The Cl₂O can be absorbed in a solvent such as CCl₄ or in water to produce a hypochlorous acid solution.

Analysis

Dichlorine monoxide can be quantitatively determined alone or in admixture with Cl₂, by iodometry; the acid consumed is a direct measure of Cl₂O (65). The reactions involved are



Hypochlorous acid reacts similarly to Cl₂O and cannot be distinguished from Cl₂O by wet analysis. Gaseous mixtures of Cl₂, Cl₂O, and HOCl can be analyzed by mass spectrometry (66,67), by ir (68), or by uv spectrophotometry (9,66,69). Gas chromatography can be used to analyze mixtures of air, Cl₂, and Cl₂O (54).

Uses

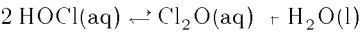
Dichlorine monoxide is an intermediate in the manufacture of calcium hypochlorite. It has been used in sterilization for space applications (70) (see STERILIZATION TECHNIQUES). Its use in the preparation of chlorinated solvents (71) and chloroisocyanurates has been described. Chlorine monoxide has been shown to be effective in bleaching of pulp (qv) and textiles (72–74).

HYPOCHLOROUS ACID

Hypochlorous acid [7790-92-3] is a highly reactive and relatively unstable compound known both in solution and in the gas phase. In solution it is the most stable and the strongest of the hypohalous acids and is one of the most powerful oxidants among the chlorine oxy-acids. It is an intermediate in the manufacture of hypochlorites. Generated *in situ* via chlorine hydrolysis, it is also an intermediate in the production of chlorohydrins (qv) and chloroisocyanurates. It is the active species that kills bacteria and other microorganisms in municipal water treatment or in swimming pool sanitation when Cl₂, hypochlorites, or chloroisocyanurates are used (75) (see WATER; BLEACHING AGENTS).

Physical Properties

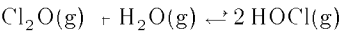
Hypochlorous acid is a weak acid with a dissociation constant $K_a = 2.90 \times 10^{-8}$ at 25°C. The temperature dependence (T in K) is given by $\log K_a = 0.0253T + 3000/T - 10.0686$ (76). Hypochlorous acid is an order of magnitude weaker than carbonic acid. The dissociation energy of HOCl from the latter study is 16.3 kJ (3.9 kcal), which is in reasonable agreement with the value of 15.1 kJ (3.6 kcal) based on the heat of neutralization (77). Dilute HOCl solutions are colorless; at higher concentrations the color ranges from yellow to yellow—orange probably because of small equilibrium amounts of Cl₂O.



The equilibrium constant at 0°C is 3.55×10^{-3} . At 0°C a 5% solution contains <0.05% Cl₂O and a 25% solution contains <1% Cl₂O.

The phase diagram of aqueous HOCl–Cl₂O shows a eutectic at –40°C (11.7 mol % Cl₂O) (3). Below the eutectic concentration the solid phase in equilibrium with the liquid phase is ice and at higher concentrations the solid phase is HOCl·2H₂O. Liquid Cl₂O and aqueous HOCl are only partially miscible. Mixing stoichiometric amounts of Cl₂O and water does not give pure HOCl but results instead in separation of two liquid phases, which on freezing give the solid compound HOCl·2H₂O.

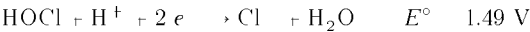
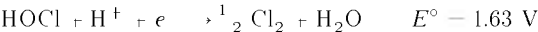
Hypochlorous acid and chlorine monoxide coexist in the vapor phase (78–81). Vapor pressure measurements of aqueous HOCl solutions show that HOCl is the main chlorine species in the vapor phase over <1% solutions (82), whereas at higher concentrations, Cl₂O becomes dominant (83). The equilibrium constant at 25°C for the gas-phase reaction, determined by ir and uv spectrophotometry and mass spectrometry, is ca 0.08 (9,66,67,69). The forward reaction is much slower than the reverse reaction.



Carbon tetrachloride extracts chlorine monoxide but not HOCl from concentrated HOCl solutions. For the equilibrium, Cl₂O(aq) ⇌ Cl₂O(CCl₄), the partition coefficient at 0°C is 2.22 (55,84).

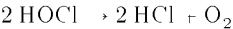
The thermodynamic properties of aqueous HOCl are $\Delta H_f^\circ = -120.9$ kJ mol⁻¹ (–28.9 kcal mol⁻¹); $\Delta G_f^\circ = -79.9$ kJ mol⁻¹ (–19.1 kcal mol⁻¹); and $S^\circ = 142.3$ J (molK) [34 cal (molK)] (85). The structure of HOCl in the vapor phase, determined by infrared and microwave spectroscopy, shows $d_{\text{O–H}} = 0.097$ nm, $d_{\text{Cl–O}} = 0.169$ nm, and ∠H–O–Cl = 104.8° (79,80). It closely resembles water in bond angle (104.7°) and O–H bond length (0.096 nm), and Cl₂O in Cl–O bond length (0.170 nm). The uv absorption spectrum of aqueous HOCl shows a maximum at 235 nm with a molar absorptivity of 100 cm⁻¹ (69,76). The infrared spectrum of gaseous HOCl shows absorption bands at 740, 1240, 2480, 3600, and 7024 cm⁻¹ (68,86).

The standard electrode potentials for the reduction of HOCl in acid solution are given below (87).



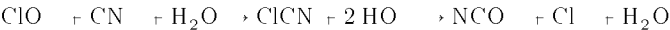
Chemical Properties

Dilute aqueous hypochlorous acid solutions are quite stable if pure, especially if kept cool and in the dark. For example, at 0°C the decomposition rate of a 1 M solution is only about 0.3% d. At 20°C the decomposition rate is about tenfold higher. Decomposition produces oxygen, chloric acid, and chlorine.



The intermediate HClO₂ is rapidly oxidized to chloric acid. Some chlorine dioxide may also be formed. Kinetic studies have shown that decomposition to O₂ and chloric acid increase with concentration, temperature (88), and exposure to light (89–92), and are pH dependent (93). Decomposition to O₂ is also accelerated by catalysts, and decomposition to chlorate is favored by the presence of other electrolytes, eg, sodium chloride (94–96).

Aqueous chlorine oxidizes numerous inorganic substrates. However, since HOCl and ClO⁻ coexist over a wide pH range, kinetic studies are necessary to establish their respective roles; both species are seldom active in the same reaction (97). The oxidation of CN⁻ is an important reaction in the treatment of waste-water and proceeds by the intermediate ClCN (98).

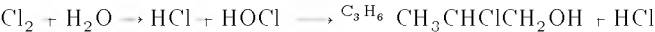


Cyanate can be further oxidized by HOCl to nitrogen and bicarbonate along with small amounts of N₂O and NCl₃. Hypochlorous acid reacts with peroxide with evolution of oxygen by the postulated intermediate formation of peroxyhypochlorous acid (99).



Hypochlorous acid reacts very rapidly and quantitatively with a slight excess of free ammonia forming monochloramine, NH₂Cl, which reacts at a slower rate with additional HOCl forming dichloramine, NHCl₂. Trichloramine is formed when three moles of HOCl are added per mole of ammonia between pH 3–4 (100). Hypochlorous acid in the form of chlorine or hypochlorite is used in water treatments to oxidize ammonia by the process of break-point chlorination, which is based on formation of unstable dichloramine. The instability of NHCl₂ is caused by presence of HOCl and NCl₃ (101,102). The reaction is most rapid at a pH of about 7.5 (103). Other nitrogen compounds such as urea, creatinine, and amino acids are also oxidized by hypochlorous acid, but at slower rates. Unstable N-chloro compounds are intermediates in deamination of amino acids (104,105).

Hypochlorous acid undergoes a variety of reactions with organic substances including addition, oxidation, C- and N-chlorination, and ester formation. On an industrial scale, hypochlorous acid, generated *in situ* via chlorine hydrolysis, reacts with propylene forming primarily the α-propylene chlorohydrin isomer.



Dichlorides and ethers are the main by-products in this reaction. Treatment with base produces propylene oxide. Specialty epoxides, eg, butylene oxide, are also produced on an industrial scale by means of HOCl generated from calcium hypochlorite and acetic acid followed by dehydrohalogenation with base.

Addition of HOCl to vinyl chloride yields chloroacetaldehyde (106); addition to acetylenic compounds produces dichloroketones (107) (see ACETYLENE DERIVED CHEMICALS).



Hypochlorous acid adds to oximes of cyclic ketones forming intermediate α-chloronitroso compounds that can be converted to nitro compounds (108).

Secondary alcohols are oxidized at room temperature to ketones in high yields by HOCl generated *in situ* from aqueous NaOCl and acetic acid (109,110). Selective oxidation in the presence of a primary alcohol is possible. In methanol, aldehydes are oxidized to methyl esters (110). Under the proper conditions, alcohols can be esterified with HOCl forming isolable alkyl hypochlorites.

Reaction of HOCl, formed from calcium hypochlorite and CO₂, with highly substituted alkenes in CH₂Cl₂ is a convenient route to allylic chlorides (111). Ketones are chlorinated to α-chloroketones by reaction with HOCl. Acetone initially gives CH₃COCH₂Cl (112). Methyl ethyl ketone gives 78° o CH₃CHClCOCH₃, 15° o CH₃CH₂COCH₂Cl, and 7° o dichlorides (113).

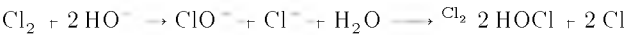
Stable N-chloro compounds are formed by reaction of hypochlorous acid and appropriate N–H compounds. For example, HOCl, formed *in situ* via chlorine hydrolysis, converts di- or trisodium cyanurates to dichloro- and trichloroiso-cyanuric acids, respectively (114). Chloroisocyanurates can also be prepared from isocyanuric acid or monosodium cyanurate and preformed HOCl (115–117). Hydrolysis of chloroisocyanurates provide HOCl for use in swimming pool disinfection and in bleaching applications.

Preparation

Chloride-containing solutions of HOCl are readily prepared by reaction of Cl₂ with H₂O or base and can involve rapid hydrolysis (118,119) or reaction with OH⁻; (120).



A saturated solution of Cl₂ (0.091 M) at 101 kPa (1 atm) and 25°C is ~6% hydrolyzed to HOCl. When Cl₂ is added to strong bases such as caustic or lime the reaction occurs stepwise. With weak bases such as NaHCO₃ or CaCO₃, a significant amount of hypochlorite is not formed as an intermediate product.



Although NaCl or CaCl₂ increase the decomposition rate of HOCl, the solutions can be utilized for synthetic and manufacturing purposes, especially if used promptly and kept cold and relatively diluted.

Chlorination of bismuth or mercuric oxides results in precipitation of relatively insoluble basic chlorides, ie, BiOCl and HgO·HgCl₂. However, the reaction with Bi₂O₃ is slow and does not produce high concentrations of HOCl (121). With HgO, the HOCl solutions may contain significant amounts of dissolved Hg.

Dilute (1–3° o), chloride-containing solutions of either HOCl, hypochlorite, or aqueous base, can be stripped in a column against a current of Cl₂, steam, and air at 95–100°C and the vapors condensed giving virtually chloride-free HOCl solutions of higher concentration in yields as high as 90° o (122–124). Distillation of more concentrated solutions requires reduced pressure, lower temperature, and shorter residence times to offset the increased decomposition rates.

A former commercial process for producing aqueous HOCl, was based on the reaction of chlorine and water vapor with sodium carbonate in either a tower or a rotating tubular reactor (61). The resulting gas stream containing Cl₂, Cl₂O, HOCl, and CO₂ was scrubbed in cold water to give 10–15° o HOCl solutions containing some chloride. Today dilute solutions of HOCl are prepared by reaction of an equilibrated mixture of chlorine gas and steam with a metal carbonate in a fluidized bed and scrubbing the gases with water in an absorber (62,125).

Virtually chloride-free solutions of HOCl are obtained by reaction of atomized 50° o caustic with excess gaseous chlorine at temperatures above the dew point of the system. The reactor gases, containing Cl₂, Cl₂O, HOCl, and H₂O are condensed to provide HOCl solutions of up to 60° o concentration in high yield. The noncondensed gases are recycled to the reactor. The free-flowing solid NaCl by-product, containing small amounts of chlorate, is recycled to a chloralkali cell (126,127). Chloride-free HOCl solutions can also be produced by passing chlorine gas over the surface of a stirred 50–60° o NaOH solution and scrubbing the off-gases, containing Cl₂, Cl₂O, and HOCl, in cold water (128).

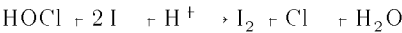
Reduced pressure distillation of a mixture of chlorine octahydrate and HgO provides a distillate with about 25° o HOCl (55,129). Chloride-free aqueous solutions of up to 76° o HOCl can be obtained by dissolving liquid Cl₂O, prepared by reaction of Cl₂ and HgO, in the appropriate amount of water (3). Alternatively, the gaseous Cl₂O can be absorbed in cold water to give lower concentrations of HOCl. In addition, a Cl₂O solution in CCl₄ can be extracted with H₂O to give Cl⁻; and Cl₂-free HOCl solutions of up to 5 M (51).

Preparation of aqueous HOCl substantially free of Cl⁻; from either aqueous Cl₂ or HOCl—salt solutions has been accomplished by electrodialysis (qv) using semipermeable membranes (130). This method has limited potential because of the unavailability of stable anionic membranes.

Organic solutions of HOCl can be prepared in near quantitative yield (98–99° o) by extraction of Cl⁻; -containing aqueous solutions of HOCl with polar solvents such as ketones, nitriles, and esters (131). These organic solutions of HOCl have been used to prepare chlorohydrins (132) and are especially useful for preparation of water-insoluble chlorohydrins. Hypochlorous acid in methyl ethyl ketone has also been used to prepare Ca(OCl)₂, by reaction with CaO or Ca(OH)₂ (133), and hydrazine by reaction with NH₃ (134).

Analysis

The analysis of HOCl is usually carried out using acidic KI as described under Cl₂O. Any chlorine present liberates iodine without consumption of acid. Chlorate does not interfere.



Hypochlorous acid can be distinguished from other chlorine species by amperometry using a membrane electrode (135). Spectrophotometry can also be used to measure HOCl via its absorbance maximum at 235 nm. Gaseous mixtures of Cl₂, Cl₂O, HOCl can be analyzed by mass spectrometry.

Uses

Hypochlorous acid, preformed or generated *in situ* from chlorine and water, is employed in the manufacture of chlorohydrins (qv) from olefins, en route to epoxides, and in the production of chloramines (qv), especially chloroisocyanurates from cyanuric acid (see CYANURIC AND ISOCYANURIC ACIDS).

HYPOCHLORITES

Metal Hypochlorites

Some hypochlorites, either as solutions or solids, are much more stable than hypochlorous acid, and because of their high oxidation potential and ready hydrolysis to the parent acid, find wide use in bleaching and sanitizing applications. One of the novel uses of hypochlorites was for disinfection of Apollo Eleven on its return from the moon (136).

The only known stable solid neutral hypochlorites are those of lithium, calcium, strontium [14674-76-1], and barium [13477-10-6]. Calcium also forms two stable basic hypochlorites (calcium hydroxide hypochlorites): Ca(OCl)₂·0.5Ca(OH)₂ [62974-42-9] and Ca(OCl)₂·2Ca(OH)₂ [12394-14-8]. Sodium hypochlorite [7681-52-9] does not have good stability. Potassium hypochlorite [7778-66-7] exists only in solution. Attempts to isolate the solid have

resulted in decomposition (137). Neutral magnesium hypochlorite [10233-03-1] has not been isolated (138), but two stable basic hypochlorites have been prepared. Impure silver (139) and basic zinc hypochlorite (140) compositions have been prepared.

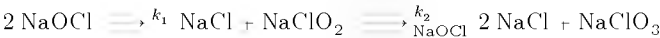
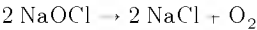
Calcium hypochlorite is the principal commercial solid hypochlorite; it is produced on a large scale and marketed as a 65–70% product containing sodium chloride and water as the main diluents. A product with a significantly higher available chlorine, av Cl₂, (75–80%) has been introduced by Olin. Calcium hypochlorite is also manufactured to a smaller extent as a hemibasic compound (~60% av Cl₂) and to a lesser extent in the form of bleaching powder (~35% av Cl₂). Lithium hypochlorite is produced on a small scale and is sold as a 35% assay product for specialty applications. Small amounts of NaOCl are employed in the manufacture of crystalline chlorinated trisodium phosphate [56802-99-4].

PROPERTIES

The solubilities of Li, Na, and Ca hypochlorites in H₂O at 25°C are 40, 45, and 21%, respectively. Solubility isotherms in water at 10°C have been determined for the following systems: Ca(OCl)₂–CaCl₂, NaOCl–NaCl, and Ca(OCl)₂–NaOCl (141). The densities of approximately equimolar solutions of NaOCl and NaCl are given in several product bulletins (142). The uv absorption spectrum of ClO[•]; shows a maximum at 292 nm with a molar absorptivity of 350 cm^{–1} (75). Heats of formation of alkali and alkaline earth hypochlorites are given (143). Thermodynamic properties of the hypochlorite ion are: Δ*H*_f[°] 107.1 kJ mol^{–1} (25.6 kcal mol^{–1}); Δ*G*_f[°] –36.8 kJ mol^{–1} (–8.8 kcal mol^{–1}); and *S*[°] 41.8 J (mol·K) (10 cal (mol·K)) (85). The reduction potential of ClO[•]; in basic solution is ClO[•] + H₂O + 2 e[–] → Cl[–] + 2 OH[–], *E*[°] 0.89 V (87).

Chemical Properties.

In Solution. Although hypochlorite solutions are much more stable than HOCl, they are subject to decomposition, which is influenced by concentration, ionic strength, pH, temperature, light, and impurities. Decomposition occurs in two ways:



The rate-controlling step to chlorate is the bimolecular formation of chlorite, which reacts rapidly with hypochlorite. The temperature dependence of the rate constants is expressed by the equations: *k*₁ = 2.1 × 10¹² e^{–103,8/RT} and *k*₂ = 3.2 × 10¹¹ e^{–87,0/RT} L (mols)^{–1} (144). The uncatalyzed decomposition to oxygen is bimolecular with an activation energy of 111.3 kJ mol^{–1} (26.6 kcal mol^{–1}). Although it is much slower than chlorate formation, it is susceptible to catalysis by trace metal impurities (145–148). The most powerful catalysts for accelerating the decomposition to oxygen are Co, Ni, and Cu; Fe and Mn are much less effective. Although these metals do not catalyze chlorate formation, iridium apparently does (149).

Hypochlorites yield HOCl when treated with stoichiometric amounts of acid and are converted to Cl₂ when excess HCl is used. They react quantitatively with iodide in acid media liberating iodine and with hydrogen peroxide liberating oxygen. These two reactions are employed in the analysis of hypochlorites. The oxidation of various inorganic anions by hypochlorite has been studied kinetically (97). Hypochlorite is a strong oxidant capable of oxidizing MnO₄^{2–}; to MnO₄[–]; IO₃[–]; to IO₄[–]; and Fe³⁺ to FeO₄^{2–}; Its reaction with ammonia to form monochloramine is the basis of the manufacture of hydrazine (qv).



Hypochlorite ion acts as a chlorinating and oxidizing agent toward organic compounds. In addition to its use in the preparation of carboxylic acids by the haloform oxidation, and amines by the Hoffmann rearrangement, it has numerous interesting and useful synthetic applications (150). Aromatically bound methylene groups in acetyl substituted aromatics are oxidized by NaOCl to carboxylic acids (151). Acetylenic protons are displaced to give chloroacetylene (152–154). Cyclopentadiene and indene are readily chlorinated by hypochlorite to perchlorocyclopentadiene (155) and 1,1,3-trichloroindene (156), respectively. Aliphatic oximes (157) and primary and secondary nitro compounds (158) are converted to geminal chloro nitro alkanes. Symmetrical dialkyl hydrazines and methylenediamine sulfate are oxidized to azo compounds (159) and diaziridine (160), respectively. *o*-Nitroanilines are oxidized in good yields by alkaline hypochlorite to benzofurazan oxides. 2,4-Dinitroaniline, on treatment with NaOCl in alkaline methanol, is converted to 5-chloro-4-methoxybenzofurazan-1-oxide via a haloalkoxy substitution reaction (161); the haloalkoxy reaction has been applied to additional heterocycles, eg, 6-nitroanthroxanic acid (162).

Hypochlorite readily chlorinates phenols to mono-, di-, and tri-substituted compounds (163). In wastewater treatment chlorophenols are degraded by excess hypochlorite to eliminate off-flavor (164). Hypochlorite converts bromobenzene to chlorobenzene in a biphasic system at pH 7.5–9 using phase-transfer catalysts (165).

Saturated hydrocarbons can be chlorinated in moderate yields under mild conditions in a biphasic system consisting of alkaline hypochlorite solution and CH₂Cl₂ containing Ni(II) bis(salicylidene)ethylenediamine as chlorination catalyst and hexadecyltrimethylammonium bromide as phase-transfer catalyst (166).

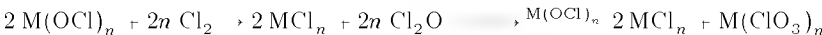
Unsaturated aldehydes, ketones, and nitriles are epoxidized in one step in high yield via nucleophilic attack by hypochlorite ion (167–170). Alkenes are epoxidized in good yield by hypochlorite in water–CH₂Cl₂ using Mn(II) porphyrins as epoxidation catalysts and triethylbenzylammonium chloride as phase-transfer catalyst (171). Manganese(III) porphyrin bound to colloidal anion exchange particles was a more effective catalyst for epoxidation of styrene by alkaline ClO[•]; than in aqueous solution (172). Olefins dissolved in methylene chloride are epoxidized at room temperature by aqueous hypochlorite using Ni(II) bis(salicylidene)ethylenediamine as epoxidation catalyst and tributylbenzylammonium chloride as phase-transfer catalyst (173,174).

Secondary alcohols are oxidized to ketones in good yields under mild conditions in a triphasic system using an inert solvent, solid Ca(OCl)₂, and a hypochlorite resin as catalyst (175).

Solid State. The stability of neutral calcium hypochlorite is primarily a function of moisture, lime, impurities, and temperature. Product containing ~7% water may lose 2–3% av Cl₂ during the first year when stored in warehouses without temperature control in moderate climates. Decomposition produces CaCl₂, Ca(ClO₃)₂, and O₂.

Heating calcium hypochlorite in a stream of N₂ during dta results in dehydration at 65–70°C; further heating causes exothermic decomposition at 200–210°C forming CaCl₂, O₂, and small amounts of Ca(ClO₃)₂. Heating Ca(OCl)₂ under conditions that do not allow complete dehydration results in decomposition at lower temperatures giving higher yields of Ca(ClO₃)₂.

Anhydrous hypochlorites are oxidized to chlorates by Cl₂O (176). The rate of chlorate formation decreases in the order Na > Ba > Sr > Li > Ca. In the presence of gaseous chlorine, dry hypochlorites decompose in two ways:



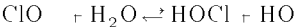
Strontium, Li, and Ca hypochlorites react primarily by the first path and NaOCl mainly by the second. In the presence of moisture, chlorate formation is the predominate reaction in all cases.

Analysis. The available chlorine (av Cl₂) in hypochlorite solutions or solids is determined by reaction with aqueous KI, followed by acidification with either acetic or sulfuric acid and titration of the liberated iodine with standard thiosulfate. The av Cl₂ in a hypochlorite is a measure of the oxidizing capacity expressed in terms of elemental chlorine; one hypochlorite ion is equivalent to one Cl₂ molecule. Thus pure Ca(OCl)₂ has an av Cl₂ of 2 × mol wt

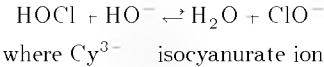
Cl₂ mol wt Ca(OCl)₂ or (2 × 70.9 143.0) × 100% 99.2% . A 5° solution of Ca(OCl)₂ contains 4.96° or ~53 g L av Cl₂.

Germicidal Properties. The germicidal activity of aqueous chlorine is attributed primarily to HOCl. Although the detailed mechanism by which HOCl kills bacteria and other microorganisms has not been established, sufficient experimental evidence has been obtained to suggest strongly that the mode of action involves penetration of the cell wall followed by reaction with the enzymatic system. The efficiency of destruction is affected by temperature, time of contact, pH, and type and concentration of organisms (177).

Although the hypochlorite ion itself is a relatively poor disinfectant (178) in comparison to hypochlorous acid, it serves as a reservoir of the latter by hydrolysis:



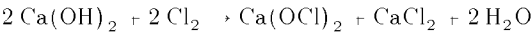
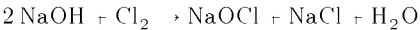
The relative concentrations of ClO⁻ and HOCl are a function of pH. The HOCl fraction is given by: HOCl / (HOCl + ClO⁻) = 1 / (H⁺ / K_a + 1)⁻¹. At 25°C it is 0.50 at pH 7.54. This is within the usual operating pH range of 7.2–7.6 for swimming pool water. For adequate germicidal activity, the free av Cl₂ (HOCl + ClO⁻) should be maintained at 1.0 ppm. The hypochlorite ion absorbs uv light in the range of 250–350 nm and therefore can be decomposed by sunlight into O₂, Cl⁻, and ClO₃⁻. Addition of cyanuric acid decreases this decomposition by formation of a chloroisocyanurate that reduces the concentrations of HOCl and ClO⁻; but hydrolyzes rapidly to maintain the equilibria:



The equilibrium constant for the first reaction is 2.40 × 10⁻⁶ at 25°C (179). When cyanuric acid is used in conjunction with a hypochlorite for sanitizing swimming pool water, the free available chlorine is kept in the 1 to 3 ppm range.

PREPARATION

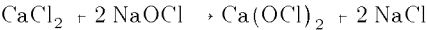
Hypochlorite solutions are prepared in near quantitative yield by chlorination of dilute caustic or a lime slurry.



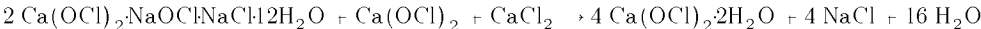
These solutions are employed in concentrations of 3–15° in various bleaching and sanitizing applications. Chlorination of 50° caustic and removal of precipitated salt produces a concentrated, low salt solution (32° NaOCl, 6° NaCl), which is used as a process intermediate in Ca(OCl)₂ manufacture. Concentrations as high as 45° can be obtained by melting NaOCl·5H₂O crystals recovered by cooling this solution.

In the preparation of a solid hypochlorite, particularly neutral Ca(OCl)₂, the presence of the coproduct CaCl₂ is undesirable because it prevents formation of large, easy-to-filter crystals of Ca(OCl)₂, and owing to its hygroscopicity, it impedes drying and has an adverse effect on product stability. Industrial processes, therefore, are designed to eliminate or minimize CaCl₂ during processing and in the final product (see CALCIUM COMPOUNDS). Strong NaOCl and dibasic and hemibasic calcium hypochlorite have been used as intermediates to remove CaCl₂ from the process. Dibasic calcium hypochlorite has also been employed as an intermediate in many processes for recovery of hypochlorite filtrate values. Because of their relatively large size, dibasic crystals allow removal of finely suspended impurities thus allowing use of less pure limes. Many processes use caustic so that sodium chloride rather than calcium chloride is the by-product (180). Various strategies for removal of NaCl from the process are employed, eg, use of triple salt, strong low salt NaOCl solutions, dibasic salt, and classification of Ca(OCl)₂–NaCl slurries. Use of HOCl can obviate the need for removal of by-product salts. The objective is to produce a high assay product while recycling by-products and minimizing waste streams.

The calcium chloride content of Ca(OCl)₂ slurries or filter cakes can be reduced or eliminated by reaction with concentrated, low salt NaOCl solution (181).



Chlorination of lime slurried in strong NaOCl solution, followed by cooling to 15°C, precipitates about 80° of the av Cl₂ as large hexagonal crystals of a triple salt: Ca(OCl)₂·NaOCl·NaCl·12H₂O [64147-46-2] (182). The recovered triple salt, free of much of the lime impurities, is treated with chlorinated lime slurry to produce neutral calcium hypochlorite dihydrate crystals [22464-76-2].



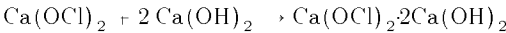
Numerous references to this compound as a 2.5 hydrate (183) or trihydrate (184) are because of the presence of occluded mother liquor. Since the salt remains in solution much of it is removed in filtration of the final Ca(OCl)₂ paste; the dried product contains about 70° av Cl₂.

Lime slurry is chlorinated in the presence of Ca(OCl)₂ mother liquor, NaOH, and NaOCl (185). After concentration, the resulting slurry of Ca(OCl)₂·2H₂O is filtered and the cake dried. A portion of the filtrate is treated with caustic, the recovered lime is recycled, and the mother liquor used to prepare the required NaOCl solution in an evaporator–chlorinator, which after separation of salt, is sent to the main reactor. In a slightly modified version, a lime purification step is added (186).

Chlorination of thick lime slurry at 40–45°C forms large crystals of hemibasic calcium hypochlorite. The fine crystals obtained under 30°C are difficult to filter and since they invariably contain occluded mother liquor, they have frequently been incorrectly referred to as monobasic or two-thirds basic (187,188). The isolated hemibasic crystals are suspended in a thin chlorinated lime slurry and chlorinated, producing laminar crystals of Ca(OCl)₂·2H₂O, which are filtered and dried. Mother liquors are treated with a lime slurry to recover the dibasic crystals, which are then suspended in a liquor of lower CaCl₂ content and chlorinated to form the neutral salt (188–190).

Other processes also use the dibasic salt as an intermediate. Dibasic calcium hypochlorite can be prepared from filtrates from chlorinated lime slurries in various ways. In one process, the filtrate is returned to the slurry being chlorinated to keep it thin. This is designed to improve crystal growth. The dibasic crystals, together with water, are added to the slurry during chlorination and some dibasic salt is prepared by chlorination in addition to the dibasic salt made from filtrates (188). In another process, dibasic crystals are separated, slurried in water, and chlorinated to obtain a slurry of neutral Ca(OCl)₂·2H₂O in a mother liquor of reduced calcium chloride content which is then filtered and air dried (191,192).

In a process formerly operated by Pennwalt, lime slurry is chlorinated to produce a solution with equimolar amounts of Ca(OCl)₂ and CaCl₂ that is sent to a crystallizer where dibasic crystals are formed.



Addition of NaCl decreases the solubility of Ca(OCl)₂ in equilibrium with the dibasic salt and lime. The dibasic slurry is sent to a classifier. Finely suspended lime impurities are removed from the overheads yielding a clear liquor, which is recycled to the lime slurry makeup. The bottoms from the classifier are chlorinated giving a slurry of Ca(OCl)₂·2H₂O, which is centrifuged. The cake is mixed with strong, low salt NaOCl solution in a pug mill and

dried. The centrate is returned to the dibasic crystallizer (183,193,194).

In another process, hypochlorite filtrate is treated with lime slurry to precipitate dibasic crystals that are filtered. The filtrate is mixed with strong caustic, chlorinated, and filtered to remove NaCl crystals. The filtrate containing Na and Ca hypochlorite is mixed with dibasic crystals and chlorinated producing a slurry of Ca(OCl)₂·2H₂O that is filtered; the cake goes to a dryer and the filtrate to the dibasic crystallizer (195).

A number of patents utilize dibasic calcium hypochlorite and concentrated NaOCl solution to produce Ca(OCl)₂·2H₂O. Coarse dibasic crystals suspended in dibasic mother liquor and concentrated NaOCl solution are chlorinated yielding a slurry of Ca(OCl)₂·2H₂O that is filtered and dried. The filtrate is recycled to the dibasic crystallizer. Lime impurities are removed by filtration of chlorinated dibasic fines (196). Clarified chlorinated lime solution can be substituted for the dibasic mother liquor (197). Alternatively, solid lime can be fed to the paste chlorinator (198).

Two cocrystallization processes employ dibasic crystals as intermediates. The PPG process (199–202) is discussed under commercial processes. The PPC process (203) forms dibasic crystals from lime and recovered filtrates. The dibasic crystals are separated from their mother liquor by decantation, slurried in caustic solution and chlorinated to produce a cocrystalline slurry of Ca(OCl)₂ and NaCl. The slurry is sent to a flotation cell where the larger salt crystals settle out and the smaller hypochlorite crystals float to the top with the aid of air and flotation agent. The hypochlorite slurry is centrifuged; the cake going to a dryer and the centrate to the flotation cell. The salt-rich bottoms from the flotation cell are centrifuged and washed with dibasic mother liquor. The centrates are recycled to the precipitation step.

Several modifications of the preparation of neutral Ca(OCl)₂·2H₂O do not involve intermediates. In a continuous process, lime slurry containing caustic and Ca(OCl)₂ mother liquor is chlorinated under reduced pressure to remove the heat of reaction, and the resulting slurry is separated in a classifier into Ca(OCl)₂– and NaCl-rich regions from which slurry is withdrawn to obtain Ca(OCl)₂ filter cake and solid salt (204).

In a batch process, NaOH is chlorinated in the presence of recycled neutral Ca(OCl)₂ mother liquor. After separation of salt, lime slurry is added and chlorinated (205). The Ca(OCl)₂·2H₂O crystals are recovered by filtration. In another version, classification of the Ca(OCl)₂–NaCl slurry gives a Ca(OCl)₂-rich fraction that is filtered and the filtrate recycled along with the NaCl-rich fraction to the first chlorinator (206). Also, 50° NaOH and solid slaked lime are used in the second chlorination.

In another cocrystallization process, lime is mixed with 50° caustic and recycled filtrate and chlorinated to yield a slurry of calcium hypochlorite dihydrate and NaCl crystals that are separated in a hydraulic classifier. The underflow is mixed with centrate mother liquor and sent to a wet screen classifier; the overflow is recycled to the hydroclone and the salt-rich bottoms are centrifuged. The centrate is recycled to the chlorinator and the salt used as feed to chloralkali cells. The Ca(OCl)₂-rich overheads from the hydroclone are centrifuged, the cake going to a dryer and the filtrate sent to the wet screen classifier (207).

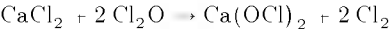
The problem of CaCl₂ formation is circumvented by use of hypochlorous acid essentially free of chloride and chlorine and treating it with hydrated lime. A PPG process is based on hypochlorous acid (208).



Carbon dioxide, containing about 10° chlorine (about an eightfold excess) and saturated with water vapor at 20–30°C, is passed through a rotating tubular reactor countercurrent to a flow of Na₂CO₃·H₂O. The exit gas containing 1–2° Cl₂O (and HOCl) is scrubbed in water forming an HOCl solution of about 10–15°. The excess Cl₂, along with most of the CO₂ is recycled; some CO₂ is purged from the system. The HOCl reacts with lime slurry at 10.0–10.5 pH producing a Ca(OCl)₂ solution of ca 15–20°. Sodium hypochlorite solution can be added to reduce the CaCl₂ concentration (209). This solution is spray dried to a product with an intermediate water level. The product can be mixed with salt, compacted, granulated, and dried further.

Significant improvements over the PPG process involve reaction of lime with concentrated HOCl (50°) and drying of the resultant slurry in a spray grainer or fluidized-bed spray dryer to produce hydrated product with av Cl₂ as high as 82° (126,127,129,210,211).

Calcium hypochlorite can also be prepared by reaction of solid lime (212), quicklime (213), or CaCl₂ (214) with Cl₂O; chlorate formation is a competing side reaction.



Crystal growth modifiers have been employed to improve filterability and water retention of Ca(OCl)₂·2H₂O, which typically crystallizes as fine plates. Addition of zinc dust or salts produces larger square- and diamond-shaped, untwinned dihydrate crystals (215). Coarse prismatic crystals are obtained by use of carbohydrates and carboxylic acids and their salts (216).

Two solvent processes for preparation of Ca(OCl)₂ have been described. In one, a CCl₄ solution of *t*-C₄H₉OCl is allowed to react with a thin lime slurry and the aqueous phase, a solution of Ca(OCl)₂, is evaporated to a product with a purity of >95% (217). In the other, a solution of HOCl in methyl ethyl ketone reacts with either CaO or Ca(OH)₂ (133). Following filtration, the residual solvent in the product is removed under vacuum.

Materials of Construction. Because of the corrosive nature of moist chlorine and hypochlorite solutions, chemically resistant materials are necessary to prevent metallic contamination of the products and to ensure proper functioning of equipment. Chlorination vessels and reactors can be constructed from fiber glass-reinforced polyester (FRP) or carbon steel with a suitable resistant coating or liner made of rubber, Saran, PVC, or poly(vinylidene fluoride) (Kynar) (see VINYL POLYMERS; VINYLIDENE POLYMERS). Although dry chlorine can be conveyed in carbon steel, moist chlorine and hypochlorite solutions require the use of solid plastic pipe or plastic-lined steel pipe. Chlorination coils or sparge tubes have been fabricated from silver, lead, glass, or PVC. However, all of these have drawbacks such as high cost, fragility, or deterioration and have been largely supplanted by solid Kynar pipe. Valves with corrosion-resistant fittings such as Teflon-lined ball valves or Kynar-lined diaphragm valves are widely employed. Hypochlorite solutions are pumped by centrifugal pumps with resistant linings such as polypropylene. Heat exchangers, cooling coils, and other equipment such as centrifuges are typically made of titanium.

HYPOCHLORITE SOLUTIONS

Sodium Hypochlorite (Liquid Bleach). Commercial strength liquid bleach used by industries, laundries, and in swimming pool sanitation, contains 12–15° av Cl₂ and is sold in 3.8- and 7.6-L polyethylene bottles and 23–57-L carboys, 205-L drums, and tank trucks of about 3-kl. capacity and greater. Household bleach contains about 5° av Cl₂ and is sold in 1–5.7-L polyethylene containers. Shipping is limited within a short radius of the plant because of transportation costs. Liquid bleach for use in chemical pulp or textile bleaching is usually prepared on site at concentrations of 30–40 g L of av Cl₂ (see BLEACHING AGENTS).

Manufacture. Sodium hypochlorite solution is usually prepared by chlorination of NaOH. Cooling is necessary, primarily for higher concentrations, since excessive temperatures can result in chlorate formation, representing loss of yield, and may contribute to lower product stability. Since chlorate formation is also a function of concentration, the upper limit of 30°C usually employed with ~6% NaOCl is reduced to about 20°C for 10–15° concentrations. The chlorination of caustic is exothermic and liberates 103.1 kJ mol (24.65 kcal mol) when gaseous Cl₂ is used. Liquid chlorine feed is preferred since advantage can be taken of its heat of vaporization, 16.5 kJ mol (3.94 kcal mol), to reduce the cooling requirement. Since 50° caustic is normally employed, and diluted to the desired strength, its heat of dilution, 20.3 kJ mol (4.86 kcal mol), is an additional cooling load. The dilution is controlled by conductivity or density. For preparation of dilute NaOCl solutions, cooling of the caustic is sufficient to absorb the heat of reaction, but for higher concentrations cooling of the hypochlorite solution is also necessary. In batch preparation of dilute hypochlorite, ice can be added directly to the

caustic to provide the necessary precooling. Although manual titration is probably still employed in some small-scale operations for determining the extent of chlorination, monitoring of the oxidation potential is not only more convenient but mandatory in continuous operation. The oxidation potential of the solution is dependent on the half cell reaction $\text{Cl}^- + 2 \text{HO}^- \rightarrow \text{ClO}^- + \text{H}_2\text{O} + 2 e^-$, and its magnitude is given by the equation $E = E^\circ - 0.0296 \log_{10} ([\text{ClO}^-] [\text{HO}^-]^2 [\text{Cl}^-])$ where E° ($- 0.89 \text{ V}$) is the standard electrode potential at 25°C when concentrations are at unit activity. Although the oxidation potential is essentially a function of pH, its measurement is preferred to pH measurement because of its faster response and lower maintenance requirements (218). The oxidation potential is measured with a potentiometer using an oxidation–reduction potential (ORP) cell consisting of a calomel or silver reference electrode and a platinum indicating electrode. Agitation of the hypochlorite solution is necessary to minimize local overchlorination and also to reduce any time lag in response of the ORP cell. Air has been used in batch operation for this purpose; however, sufficient agitation can be obtained from the turbulence of the Cl_2 feed itself or by recirculating through an external loop. Complete absorption of the Cl_2 is ensured by maintaining an adequate depth of solution in the chlorinator. In many continuous systems the Cl_2 and caustic are allowed to react in a mixing zone, which may be a packed tubular reactor, with the hypochlorite solution going either to a surge tank or to storage. The conversion of NaOH is usually limited to about 92–94% for ease of control and to avoid overchlorination. A small excess of NaOH is necessary for adequate storage stability. In certain applications, such as textile-bleaching, little or no free caustic alkalinity is desirable. In bleaching of pulp, a pH adjustment may be made to obtain the necessary degree of activity. Prior to bottling, any suspended solids are allowed to settle or they may be removed by filtration (see BLEACHING AGENTS, PULP AND PAPER).

High yields of NaOCl are obtained electrolytically by oxidation of Cl^- at dimensionally stable anodes (219). Sodium hypochlorite is prepared using small diaphragmless or membrane cells, with a capacity of 1–150 kg/d of equivalent Cl_2 , which produce a dilute hypochlorite solution of 1–3 and 5–6 g/L from seawater and brine, respectively (see CHEMICALS FROM BRINE). They are employed in sewage and wastewater treatment and in commercial laundries, large swimming pools, and aboard ships.

Calcium Hypochlorite (Bleach Liquor). Bleach liquor is a solution of $\text{Ca}(\text{OCl})_2$ and CaCl_2 containing some dissolved lime. The av Cl_2 can vary but is typically about 33–35 g/L. Although it has some disadvantages, such as scaling and water treatment problems, which are causing a slow shift to sodium hypochlorite, it has considerable use because of lower cost. It is invariably prepared on site and consumed captively primarily for chemical pulp bleaching.

Manufacture. The mechanics of the preparation of bleach liquor by chlorination of lime slurry is only slightly different than that of sodium hypochlorite, and the heat liberated per mol of chlorine is approximately the same. Continuous systems are preferred because of their lower maintenance requirements. On a sufficiently large scale a lime slaker can be justified. In general, good quality slaked lime is employed to make a thick slurry that is subsequently diluted to the desired concentration by means of a density controller. The lime slurry is conveyed to a suitable reactor, such as a tower, where it is contacted with chlorine under the control of an ORP cell. The finished bleach liquor can go to a settling tank for sludge separation or be put through a centrifugal cleaner before going to storage.

Economic Aspects. U.S. production of sodium hypochlorite has increased by ca 1% per year since 1980 (Table 4) (220). Of the 1988 production of ca 245,000 t of equivalent chlorine, 61% was industrial strength (~15% av Cl_2) and 39% household strength (~5% av Cl_2). Long-term growth in chemical pulp bleaching is expected to decline because of environmental factors and performance disadvantages compared to alternative bleaching agents. U.S. consumption of calcium hypochlorite bleach liquor amounts to over 2000 t/yr of equivalent Cl_2 , ca 53×10^6 L (14 million gallons) of liquor containing 3–3.5% av Cl_2 .

Table 4. United States Hypochlorite Production^a

Year	NaOCl, ^b 10 ³ t	Ca(OCl) ₂ , ^c 10 ³ t
1980	210–248	84–88
1981	217–255	84–88
1982	214–246	64–77
1983	216–249	64–77
1984	218–253	73–82
1985	221–255	73–82
1986	223–258	73–82
1987	226–263	75–85
1988	231–268	77–87

^a Ref. 220.

^b Metric tons of equivalent chlorine.

^c Metric tons of 65–70% av Cl_2 product.

Uses. Sodium hypochlorite is used in chemical pulp and textile bleaching where it is largely produced on site for captive consumption. It is also used as a commercial laundry and household bleach, as a sanitizer for swimming pools, and as a disinfectant for municipal water and sewage. In food processing, sodium hypochlorite is employed as a disinfectant and sanitizer. In the production of oil it is added to water used for flooding to prevent the formation of fungi, which could cause plugging. In oil refineries it is employed as a sweetening agent. Large quantities of sodium hypochlorite are used in the chemical industry, primarily for the manufacture of hydrazine (qv) as well as in the synthesis of organic chemicals. Sodium hypochlorite is also used in the manufacture of chlorinated trisodium phosphate (see BLEACHING AGENTS).

SOLID HYPOCHLORITES

Sodium Hypochlorite–Trisodium Phosphate Complex. Commercial crystalline trisodium phosphate (TSP) is a complex of the type $(\text{Na}_3\text{PO}_4 \cdot x\text{H}_2\text{O})_n\text{NaY}$ where $n = 4$ to 7, $x = 11$ or 12, and Y is a monovalent anion (see PHOSPHORIC ACIDS AND PHOSPHATES). Chlorinated trisodium phosphate is also a complex of this type with the formula $(\text{Na}_3\text{PO}_4 \cdot 11\text{H}_2\text{O})_4 \cdot \text{NaOCl}$ (221). The crystalline, efflorescent product melts at 62°C, which is really a transition to $\text{Na}_3\text{PO}_4 \cdot 8\text{H}_2\text{O}$. A high purity product can be obtained by crystallization from a liquor having the proper $\text{Na}_2\text{O}:\text{P}_2\text{O}_5$ ratio containing an excess of NaOCl. Although the calculated av Cl_2 is 4.66%, commercial material usually contains about 3.65% owing to the presence of salt as well as chlorate from decomposition of NaOCl. The loss in storage is about 0.05% av Cl_2 per month.

Manufacture. Chlorinated TSP is made batchwise by addition of a 15% NaOCl solution containing some NaOH to a hot (75–80°C) concentrated liquor consisting of di- and trisodium phosphates, in a mole ratio of about 1:10, in a suitable reactor, eg, a pan mixer (222). The mixture is allowed to cool slowly under constant agitation until crystallization occurs (62°C). When crystallization is complete, cooling is continued to about 45°C and the slightly moist crystals are air dried. Overdrying can result in decreased stability.

The product is shipped in 45-kg polyethylene-lined paper bags, 23-kg Fiberpak drums, and 57- and 136-kg Leverpak drums.

Economic Aspects. Sodium hypochlorite–trisodium phosphate complex was commercialized in 1930. Chlorinated TSP is manufactured by Stauffer (a subsidiary of Rhône-Poulenc, Inc.). The consumption, steadily decreasing since 1980, dropped sharply in 1985 because of reduced use in dishwasher detergents. The estimated demand in 1987 was 37,360 t (220). In 1988 it sold for \$0.32/lb (\$0.70/kg) for truckload quantities of 660 kg (300-lb) drums.

Applications. The principal uses are in scouring cleansers and acid metal cleaners for dairy equipment. Use in dishwasher detergents has been supplanted by chlorinated isocyanurates, which are more cost-effective, more stable in hot water, and possess water softening properties.

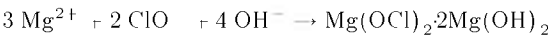
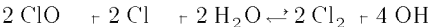
Lithium Hypochlorite. High purity, anhydrous lithium hypochlorite [13840-33-0], LiOCl, is a white, lightweight, dusty, hygroscopic, and corrosive powder. The monohydrate is free-flowing, nondusty, and of reasonable density. The presence of diluents such as salt, sodium, and potassium sulfates reduces dustiness, increases bulk density, reduces reactivity, and improves storage stability. The commercial product is marketed in this form.

Manufacture. Calcined spodumene [1302-37-0], a lithium aluminum silicate, LiAlSi₂O₆, is treated with sulfuric acid, neutralized to pH 6, and filtered to remove insolubles. The filtrate containing Li, Na, and K sulfates is treated with caustic (forming LiOH), cooled to 0°C, and filtered to separate crystallized Na₂SO₄·10H₂O. Additional caustic is added followed by chlorination and flash drying of the reaction mixture (223). Typical product analysis is LiOCl 30%_o, NaCl 34%_o, Na₂SO₄ and K₂SO₄ 20%_o, LiCl 3%_o, LiClO₂ 3%_o, LiOH 2%_o, Li₂CO₃ 1%_o, and H₂O 7%_o (224). The free-flowing product is shipped in 22.7, 45.4, and 113.4-kg fiber drums with polyethylene liners. The loss of av Cl₂ is claimed to be <3%_{yr}. Decomposition produces almost exclusively chloride and chlorate.

Economic Aspects. Lithium hypochlorite is produced by Lithium Corporation of America (a subsidiary of FMC) at its plant in Bessemer, North Carolina which has a capacity of about 4000 t_{yr}. Its total demand is low owing to its relatively high price of about \$1.27/lb in truckload quantities. Estimated U.S. consumption in 1987 was 2000–2500 t, 80–90%_o being used in swimming pool sanitation.

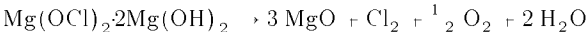
Applications. Lithium hypochlorite, first introduced in 1964, has limited use in swimming pool and spa sanitation and dry laundry bleaches.

Dibasic Magnesium Hypochlorite. Basic magnesium hypochlorite [64131-05-1], av Cl₂ ~40–45%, has been known for over 100 years and was once an item of commerce. Dibasic magnesium hypochlorite was first synthesized in 1969 by addition of either a NaOCl or Ca(OCl)₂ solution to an excess of aqueous MgCl₂ or Mg(NO₃)₂ (225). Solid hydrates or slurries can also be employed as reactants (226). The reaction proceeds as follows:



A competing side reaction is chlorate formation, 3 ClO₂ → 2 Cl₂ + ClO₃⁻, which decreases the yields of dibasic magnesium hypochlorite [11073-21-5] and of evolved chlorine. The difficult to filter slurries can be dried with little loss to a white, powdery solid with av Cl₂ in the range of 52–59%_o. The yields of isolated product and recovered chlorine are typically about 40%_o each, while product solubility loss and chlorate formation amount to about 10%_o each.

Dibasic magnesium hypochlorite is more thermally stable than neutral or dibasic calcium hypochlorite. In addition, its decomposition, which starts at ~325°C, is endothermic rather than exothermic as in the case of the Ca compounds.



By contrast, decomposition of dibasic calcium hypochlorite begins at ~265°C to give Ca(OH)₂, CaCl₂, and O₂. Dibasic magnesium hypochlorite exhibits a high degree of stability to moisture as shown by the following relative available chlorine losses at 24°C and 80%_{rh} for 60 d: Mg(OCl)₂·2Mg(OH)₂ 2%_o, Ca(OCl)₂·2Ca(OH)₂ 6%_o, and Ca(OCl)₂ 100%_o.

Dibasic magnesium hypochlorite can be used as a toilet bowl cleaner (227–229), in laundry and textile bleaches (230,231), and in scouring cleansers (232,233).

Calcium Hypochlorite. High assay calcium hypochlorite [7778-54-3] was first commercialized in the United States in 1928 by Mathieson Alkali Works, Inc. (now Olin Corp.) under the trade name HTH. It is now produced by two additional manufacturers in North America (Table 5). Historically, it usually contained about 1%_o water and 70–74%_o av Cl₂, so-called anhydrous product, but in 1970, a hydrated product was introduced (234). It is similar in composition to anhydrous Ca(OCl)₂ except for its higher water content of about 6–12%_o and a slightly lower available chlorine content. This product has improved resistance to accidental initiation of self-sustained decomposition by a lit match, a lit cigarette, or a small amount of organic contamination. U.S. production in the 1990s consists primarily of partially hydrated Ca(OCl)₂, which is sold as a 65%_o av Cl₂ product mainly for swimming pool use. Calcium hypochlorite is also sold as a 50%_o av Cl₂ product as a sanitizer used by dairy and food industries and in the home, and as a 32%_o product for mildew control.

Table 5. Calcium Hypochlorite Producers and Capacities as of 1989^a

Producer	Plant location	Capacity, 10 ³ t/yr
Olin Corp. ^b	Charleston, Tenn.	72.7
PPG Industries, Inc. ^c	Natrium, W.Va.	32.7
Saskatoon Chemical ^d	Saskatoon, Sask.	7.0
<i>Total</i>		<i>103.3</i>

^a Ref. 235.
^b Olin closed its 27.3 kt/yr Niagara Falls, N.Y. plant in 1982.
^c PPG opened its Natrium plant in 1984 and closed its 7.7 kt/y Barberton, Ohio plant.
^d Saskatoon's process is based on patents in Ref. 236–238.

Manufacture. A high purity, completely hydrated lime of high reactivity is employed in the manufacture of calcium hypochlorite. It should contain low levels of impurities such as silica, MgO, CaCO₃, CaSO₄, Al₂O₃, Fe₂O₃, and trace metals such as Co, Ni, Cu, and Mn, since some of these can cause process difficulties and can also affect the quality and stability of the final product.

Calcium hypochlorite is made by drying a filter cake of neutral calcium hypochlorite dihydrate containing 30–50%_o water depending on the type of filter used. This material is usually prepared from hydrated lime, caustic, and chlorine. The cake can be air or vacuum dried. During air drying some reaction with CO₂ occurs resulting in formation of CaCO₃. Some loss of available chlorine also occurs leading to formation of chlorate, chloride, oxygen, chlorine, and possibly HOCl and Cl₂O. Control of moisture and mechanical treatment (preforming) during drying results in a free-flowing essentially dustless granular product (182,239). Slurries containing about 45%_o solids can be sprayed into a fluidized bed of granular Ca(OCl)₂ (240). The intermediate product containing about 20%_o water can be dried further by conventional means.

Commercial Processes. Olin's earlier triple salt process, originally commercialized in 1928, was modified in 1983. In the patented process, a slurry of dibasic calcium hypochlorite is mixed with a strong, low salt sodium hypochlorite solution and hypochlorite liquors and chlorinated. The resultant Ca(OCl)₂·2H₂O slurry is filtered, the cake going to the dry-end and the filtrate to the dibasic precipitation step where it reacts with lime.

PPG formerly operated an HOCl-based process (208) that was originally commercialized in 1937. Since 1984 it has operated a cocrystallization process. According to PPG's patents, lime is slurried with dilute Ca(OCl)₂ mother liquor and precipitated as dibasic Ca(OCl)₂ by reaction with a stronger hypochlorite filtrate. After thickening in a settling tank, the dibasic slurry is mixed with 50%_o NaOH and a stronger hypochlorite filtrate and chlorinated to produce a slurry of Ca(OCl)₂ dihydrate and NaCl crystals which are classified by elutriation. The salt-rich underflow is centrifuged and the centrate used as the elutriant. The salt is reslurried in dibasic mother liquor and centrifuged to produce a salt cake; the centrate is sent to the dibasic precipitation step. The

Ca(OCl)₂-rich overflow from the classifier is pressure filtered; the filtrate goes to the dibasic precipitation step and the filter cake to a drier.

Calcium hypochlorite (65° o) contains salt and water as the main diluents along with small amounts of CaCl₂, Ca(ClO₃)₂, Ca(OH)₂, and CaCO₃. It is shipped as a granular or tableted product in polyethylene containers of various sizes from 1 to 16 kg capacity. It is also shipped in 23-, 34-, and 45-kg fiber drums with a polyethylene-coated aluminum lining and a galvanized steel cover. The product is also packaged in a polyethylene bag within a fiber drum. An epoxy-coated steel drum is also used, especially for exported materials. All-plastic drums were introduced in the early 1990s.

Economic Aspects. U.S. production statistics for the period 1980 to 1988 are given in Table 4 (220). Exports amount to ca 20° o of annual United States production, and imports amount to almost 10° o of domestic production. The main foreign producers are Japan, South Africa, and Canada. South Korea, Brazil, and The People's Republic of China are minor producers. Japan's Nippon Soda Co., Ltd. is the world's third largest producer. Two other Japanese producers are Toyo Soda Co., Ltd., and Nankai Chemical Industry, Ltd.

From 1984 to 1988, the U.S. market grew at an average rate of about 3° o yr. Consumption is expected to grow at about 4° o yr through 1993. The growth is occurring primarily in the swimming pool market; growth in the industrial sector is relatively stagnant. Calcium hypochlorite is used mainly, ca 80° o, for swimming pool sanitation where it has ~25% of the market (Table 6). In the mid-1980s calcium hypochlorite lost market share to chloroisocyanurates in the residential in-ground pool sector. However, this trend has begun to subside. The loss to isocyanurates has been offset to a minor extent by gains over liquid bleach and chlorine in public pools.

Table 6. Swimming Pool Sanitizer Use in the United States^a

Sanitizer	° o
chloroisocyanurates	28
calcium hypochlorite	25
sodium hypochlorite (solution)	24
chlorine gas	15
other ^b	7

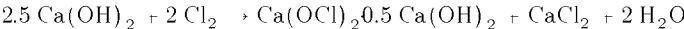
^a Ref. 235; 1988 estimates; excludes ancillaries.

^b Lithium hypochlorite, halogenated hydantoins, potassium peroxymonosulfate, and hydrogen peroxide.

Applications. Calcium hypochlorite (65–70° o av Cl₂) is used for disinfection in swimming pools and drinking water supplies. It is also used for treatment of industrial cooling water for slime control of bacterial, algal, and fungal origin, and for disinfection, odor control, and BOD reduction in sewage and wastewater effluents. Calcium hypochlorite is employed as a sanitizer in households, schools, hospitals, and public buildings. It is also used for microbial control in restaurants and other public eating places. Calcium hypochlorite is used for bacterial control, odor control, and general sanitation in dairies, wineries, breweries, canneries, food processing plants, and beverage bottling plants. It is employed as a mildew-cide in and around the home, boats, campers, and trailers (see DISINFECTANTS AND ANTISEPTICS; INDUSTRIAL ANTIMICROBIAL AGENTS).

Safety and Handling. Calcium hypochlorite is heated to about 90°C during drying and thus is stable at normal temperatures encountered in transportation, storage, and use. It decomposes exothermically when heated to ca 175°C, releasing oxygen, which will intensify a fire reaching containers of calcium hypochlorite. It should be stored in a cool, dry, and well-ventilated area. Since calcium hypochlorite can react vigorously and sometimes explosively with certain organic and inorganic materials, they should be kept away from it during shipment, storage, use, or disposal. In the event of decomposition or contamination, the container should not be resealed but should be isolated if possible and flooded with sufficient water to completely dissolve and wash away the contents.

Hemibasic Calcium Hypochlorite. This basic hypochlorite [62974-42-9] is produced by chlorination of lime. It has a lime content of ~20% and an av Cl₂ of ~60%.



Because of the simplicity of the manufacturing process it is cheaper than neutral calcium hypochlorite, and because of its higher av Cl₂ and better stability, it is a superior alternative to bleaching powder [64175-94-6].

Manufacture. Hemibasic calcium hypochlorite is manufactured by chlorination of lime slurry followed by filtration and drying of the filter cake.

Economic Aspects. The approximate annual world capacity of hemibasic calcium hypochlorite, ca 60° o av Cl₂, was 28,000 t in 1988. The principal producers are Japan and The People's Republic of China; Italy and India are minor producers (220).

Applications. Because of its high lime content, the use of hemibasic calcium hypochlorite in general sanitation is limited. It is used primarily in Japan and lesser developed countries as an alternative to bleaching powder.

Bleaching Powder. This material, known since 1798, is made by chlorination of slightly moist hydrated lime, calcium hydroxide [1305-62-0], Ca(OH)₂. It has the empirical formula Ca(OCl)₂·CaCl₂·Ca(OH)₂·2H₂O. Its composition, long a subject of controversy, was established by phase studies, microscopy, and x-ray diffraction techniques (241). The initial chlorination products are monobasic calcium chloride [14031-58-4] and dibasic calcium hypochlorite [12394-14-8]:



On further chlorination, the dibasic compound is converted to a mixed crystal consisting largely of Ca(OCl)₂. Ordinary bleaching powder is a mixture of this substance and the basic chloride. Prolonged chlorination partially converts the basic chloride to hydrated CaCl₂, but the mixed crystal persists with gradually changing properties. Heating above 40°C causes the material to lose its free-flowing and nonhygroscopic characteristics. Poor storage stability results from the presence of CaCl₂ and water. The addition of CaO to react with water improves stability; this gave rise to a so-called stabilized bleaching powder suitable for use in tropical areas. A more stable product is also obtained by mixing bleaching powder with strong NaOCl solution or by chlorination of a lime–NaOH mixture (242).

Manufacture. For bleaching powder, numerous improvements over the original chamber process were developed to deal primarily with heat and moisture removal and mechanical apparatus for batch or continuous manufacture of bleaching powder of improved quality and stability (243). For example, in a two-stage process (244), hydrated lime is chlorinated in a jacketed reactor equipped with an agitator at 20–25°C and 5.3–12.0 kPa (40–90 mm Hg) and then at 50–55°C and 4.0–6.7 kPa (30–50 mm Hg) to give a product containing 36.8° o Ca(OCl)₂, 31.7° o CaCl₂, 26.2° o Ca(OH)₂, 3.0° o CaCO₃, 0.2° o Ca(ClO₃)₂, and 0.9° o H₂O. This material, with hardly any chlorine odor, was much more stable and much less corrosive than the product (~11% H₂O) made by the older chamber process and was suitable for use in tropical climates. In less developed or remote areas, bleaching powder may still be prepared on a small scale by generating Cl₂ from MnO₂, NaCl, and H₂SO₄, and treating it with hydrated lime placed on shelves in an absorption chamber (245).

Economic Aspects. The production of bleaching powder has been steadily declining. Peak U.S. production was 133,400 metric tons in 1923; it decreased to 23,600 t in 1955 and has not been reported since. Imports, averaging 1160 t during 1980–1987, came from India, Spain, the United Kingdom, Germany, and Canada (220). It is probably also manufactured in some less developed countries.

Applications. Bleaching powder can be employed for general sanitation and may also be used to disinfect seawater, reservoirs, and drainage ditches where the volume of insolubles is not important. It can be used as a decontaminating agent for areas sprayed with chemical warfare agents such as mustard gas (see CHEMICALS IN WAR). The high insoluble (lime) content is an undesirable feature of bleaching powder owing to the loss of hypochlorite in

the sludge that is formed in aqueous slurries.

Organic and Nonmetal Hypochlorites

Alkyl hypochlorites, esters of hypochlorous acid, are nonpolar, volatile liquids with irritating odors and are extremely lachrimatory. The known alkyl hypochlorites (ROCl) are methyl (CH₃) [593-78-2], ethyl (C₂H₅) [624-85-1], *t*-butyl (*t*-C₄H₉) [507-40-4], and *t*-amyl (*t*-C₅H₁₁) [24251-12-5]. Primary and secondary hypochlorites are very unstable but tertiary hypochlorites exhibit good stability. *t*-Butyl hypochlorite has been the alkyl hypochlorite of choice for experimental work owing to its stability and ease of preparation in high yield and purity by chlorination of an alkaline solution of the alcohol. This alkyl hypochlorite is a convenient source of positive chlorine and is soluble in most organic solvents. It is used in organic synthesis because of its high selectivity as an oxidant and for *C*- and *N*-chlorinations. The low flash point (< 10°C) of *t*-C₄H₉OCl creates a potential fire hazard that can be reduced by use of inert solvents.

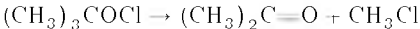
Numerous fluorinated and perfluorinated alkyl hypochlorites have been synthesized and characterized, eg, CF₃OCl [22082-78-6], C₂F₅OCl [22675-67-8], *i*-C₃F₇OCl [22675-68-9], and *t*-C₄F₉OCl [22082-78-6]. These nonmetal oxychlorine compounds are much more thermally stable than the corresponding parent compounds and can be prepared by reaction of ClF with the appropriate carbonyl compound or alcohol.

Although no acyl hypochlorites [RCO₂Cl] have been isolated in pure form, they have been characterized in solution and employed as reactants via *in situ* generation from Cl₂O or HOCl and carboxylic acids, or from Cl₂ and silver salts of carboxylic acids (246,247). Perfluoroacyl hypochlorites have also been prepared (248).

Inorganic nonmetal unipositive oxychlorine compounds include ClONO₂ (19), ClOClO₃ (249), and the hypochlorites derived from monobasic fluorine-containing oxyacids of the group VIA elements S, Se, and Te; eg, HOSO₂F (250), HOSO₂CF₃ (251), HOSF₅ (40,252), HOSeF₅ (253), and HOTeF₅ (254). In addition, two members of a new class of unipositive chlorine compounds derived from the hydroperoxides CF₃OOH and SF₅OOH have been prepared (255–258).

Physical Properties. Data on physical properties of organic hypochlorites is limited. Some boiling points and densities of alkyl hypochlorites have been published as well as data on viscosity (259), uv spectra (8) and partition coefficients between CCl₄ and water (260). The liquid-phase equilibria for the system *t*-C₄H₉OH–*t*-C₄H₉OCl–H₂O have been determined (261). Only a few boiling points have been determined for the fluoroalkyl hypochlorites. The volatilities of the fluoroalkyl hypochlorites are somewhat lower than those of the parent alcohols. Some vapor pressure data are also given as well as ir and nmr spectral data. Some physical data on the inorganic nonmetal hypochlorites and the peroxy hypochlorites are available.

Chemical Properties. The primary and secondary alkyl hypochlorites decompose vigorously on warming, and explosively when exposed to light. The principal initial thermal decomposition products are aldehydes and ketones, R₂CHOCl → R₂C=O + HCl where R = H or alkyl. Secondary reactions can occur leading to chlorination products, carboxylic acids, and their esters. In contrast, the tertiary hypochlorites are significantly more stable; *t*-butyl hypochlorite, eg, can be distilled and stored for months at ambient temperature with little or no decomposition. However, in bright sunlight it will slowly decompose giving primarily acetone and methyl chloride.



The kinetics of formation and hydrolysis of *t*-C₄H₉OCl have been investigated (262). The chemistry of alkyl hypochlorites, *t*-C₄H₉OCl in particular, has been extensively explored (247). *t*-Butyl hypochlorite reacts with a variety of olefins via a photoinduced radical chain process to give good yields of allylic chlorides (263). Steroid alcohols can be oxidized and chlorinated with *t*-C₄H₉OCl to give good yields of ketosteroids and chlorosteroids (264) (see STEROIDS). *t*-Butyl hypochlorite is a more satisfactory reagent than HOCl for *N*-chlorination of amines (265). Sulfides are oxidized in excellent yields to sulfoxides without concomitant formation of sulfones (266). 2-Amino-1, 4-quinones are rapidly chlorinated at room temperature; chlorination occurs specifically at the position adjacent to the amino group (267). Anhydropenicillin is converted almost quantitatively to its 6-methoxy derivative by *t*-C₄H₉OCl in methanol (268). Reaction of unsaturated hydroperoxides with *t*-C₄H₉OCl provides monocyclic and bicyclic chloroalkyl 1,2-dioxolanes. *t*-Butyl hypochlorite has been used for the preparation of epoxides (269).

In contrast to the alkyl hypochlorites, the fluoroalkyl hypochlorites are extremely susceptible to hydrolysis but are much more thermally stable. Trifluoromethyl hypochlorite, eg, showed no decomposition when heated for several days at 100°C. When decomposition does occur, several products are formed; C₂F₅OCl gives COF₂, CF₃Cl, CF₃COF, and ClF, whereas (CF₃)₃COCl gives (CF₃)₂CO, Cl₂, CF₃Cl, and C₂F₄ (40).

The fluoroalkyl hypochlorites readily react with CO and SO₂ to form the corresponding chloroformates and chlorosulfates in near quantitative yields (270). They add to olefins giving α-chloroethers (271). Borate esters are obtained by reaction of perfluoroalkyl hypochlorites with BCl₃ (272).



Although the perfluoroacyl hypochlorites are thermally unstable and explosive, CF₃CO₂Cl and C₃F₇CO₂Cl are easily handled and are well characterized.

Uses. *t*-Butyl hypochlorite has been found useful in upgrading vegetable oils (273) and in the preparation of α-substituted acrylic acid esters (274) and esters of isoprene halohydrins (275). Numerous patents describe its use in cross-linking of polymers (qv) (276), in surface treatment of rubber (qv) (277), and in odor control of polymer latexes (278). It is used in the preparation of propylene oxide (qv) in high yield with little or no by-products (269,279). Fluoroalkyl hypochlorites are useful as insecticides, initiators for polymerizations, and bleaching and chlorinating agents (280).

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CHLOROUS ACID, CHLORITES, AND CHLORINE DIOXIDE

Sodium chlorite [7758-19-2], NaClO₂, an oxidizing agent, is manufactured and distributed worldwide in commercial quantities as aqueous solution, flake, and powder products. The primary use for sodium chlorite is on-site generation of chlorine dioxide [10049-04-4], ClO₂, through oxidation and or acidification of an aqueous chlorite solution. Sodium chlorite is used to produce chlorine dioxide economically in quantities of less than 2000 kg d. Sodium chlorate [7775-09-9] NaClO₃, is the preferred raw material for producing larger quantities of chlorine dioxide (see CHLORINE OXYGEN ACIDS AND SALTS, CHLORIC ACID AND CHLORATES).

Chlorine dioxide is finding increasing use as an oxidizing bleaching agent in the pulp (qv) and paper (qv) industry, replacing chlorine [7782-50-5], Cl₂, and aqueous sodium hypochlorite, [7681-52-9], NaOCl (see BLEACHING AGENTS). Use of ClO₂ significantly reduces the quantity of adsorbable organically-bound halide (AOX) effluents produced in paper pulp bleaching processes. Chlorine dioxide is also increasing use as a disinfectant or biocide in municipal and industrial water (qv) treatment (see DISINFECTANTS AND ANTISEPTICS) as well as an oxidizer in oil field and pollution abatement processes (see PETROLEUM). Chlorous acid [13898-47-0], HClO₂, is a short-lived chemical intermediate generated in acidified sodium chlorite solutions and is involved in the chemistry of the production and use of chlorine dioxide in oxidation and bleaching processes.

CHLORINE DIOXIDE

Physical Properties

Chlorine dioxide, ClO₂, is a greenish yellow gas having a pungent odor that is distinctive from that of chlorine. Liquid chlorine dioxide has a deep red color and is explosive at temperatures above -40°C. Selected physical and thermodynamic properties of chlorine dioxide are given in Table 1.

Table 1. Physical and Thermodynamic Properties of Chlorine Dioxide ^a

Property value	Values
mol wt	67.452
critical temperature, K	465
critical pressure, kPa ^b	8621.6
mp, K	213.55
triple point temperature, K	213.55
triple point pressure, kPa ^b	1.2544
bp at 101.3 kPa ^b , K	284.05
liquid molar volume, m ³ kmol	4.1852×10^{-2}
density of liquid, g mL ⁻¹ 55°C	1.773
0°C	1.640
10°C	1.614
ideal gas heat of formation, kJ mol ^c	102.5
ideal gas Gibbs energy of formation, kJ mol ^c	120.5
ideal gas entropy, kJ (mol·K) ^c	0.257
standard net heat of combustion (gas), kJ mol ^c	102.5
dipole moment, Cm ^d	5.9500×10^{-30}
acentric factor	0.35638
radius of gyration, m	2.8030×10^{-10}
<i>Properties as a function of temperature</i>	
	Temperature, °C
	0°C 20°C 40°C
ideal gas heat capacity, kJ (mol·K) ^c	0.0408 0.0417 0.0425
latent heat of vaporization, kJ mol ^c	26.937 25.825 24.629
vapor pressure, kPa ^b	64.419 141.33 268.51

^a Ref. 1. All temperatures at 298.15 K unless otherwise noted.
^b To convert kPa to mm Hg, multiply by 7.501.
^c To convert J to cal, divide by 4.184.
^d To convert Cm to debyes, divide by 3.336 × 10⁻³⁰.

Chlorine dioxide exists as a free-radical monomer (2–5). The chlorine–oxygen bonds have a double-bond character (6), O–Cl–O angle of about 117.5°, and a chlorine–oxygen bond length of 0.147 nm (5,7–12). The aqueous ultraviolet absorption spectrum of chlorine dioxide has a broad absorption band. The maximum is near 360 nm and the molar extinction coefficient, given as 1150 (M·cm)⁻¹, is more accurately valued at 1250 (M·cm)⁻¹ when using high resolution, narrow bandwidth spectrophotometers (13–18). The extinction coefficient is independent of temperature from 25 to 50°C, and from acid concentrations ranging from 0.2–4 N, ionic strength, 2–4 M, and chloride ion concentrations up to 0.3 M (16). The chlorine dioxide absorption spectrum in aqueous or organic solutions is the same as the gas-phase spectrum (13).

Chlorine dioxide is soluble in water, forming a yellow to yellow-green color solution that is quite stable if kept cool and in the dark. Various crystalline hydrates of chlorine dioxide have been described including a hexahydrate (19), an octahydrate (20), and an orange colored decahydrate (21). The partition coefficient between water and ClO₂ gas is about 21.5 at 35°C and 70.0 at 0°C (22). Data on the solubility of chlorine dioxide in water at various

chlorine dioxide gas partial pressures (23) have been published. Chlorine dioxide solubilities in water at partial pressures to 20 kPa (150 mm Hg) from experimental data (24) having a better internal consistency are shown in Figure 1.

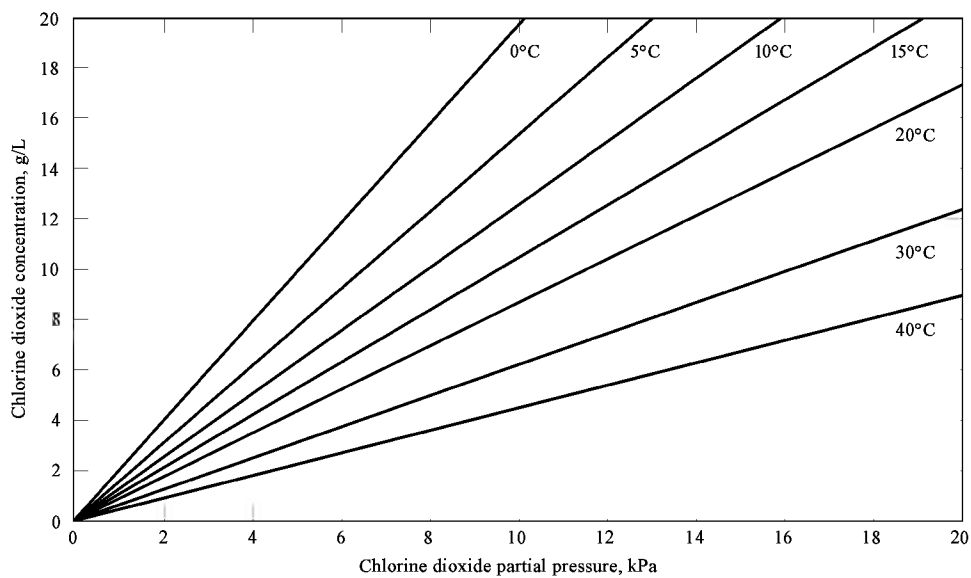


Fig. 1. Solubility of chlorine dioxide in water. To convert kPa to mm Hg, multiply by 7.501.

An equation for calculating the partial pressure of chlorine dioxide above specified chlorine dioxide solutions at various temperatures based on the data from reference 24 has been developed (25):

$$p_{\text{ClO}_2} = (\text{g L ClO}_2) e^{[10.717 - (3102/T)]} \tag{1}$$

where p_{ClO_2} is the partial pressure of chlorine dioxide gas in kPa, g L ClO₂ is the chlorine dioxide solution concentration in grams per liter, and T is the absolute temperature in Kelvin. Reference 24 gives chlorine dioxide partial pressure values that are about 10–12% higher than those of reference 23.

Chemical Properties

Chlorine dioxide gas is a strong oxidizer. The standard E° reversible potential is determined by the specific reaction chemistry. The standard E° potential for gaseous ClO₂ in aqueous solution reactions where a chloride ion is the product is 1.511 V, but the potential can vary as a function of pH and concentration (26):



$$E = 1.511 + 0.0473 \text{ pH} - 0.0118 \log \left\{ \left(p_{\text{ClO}_2} \right) \left[\text{Cl}^- \right] \right\} \tag{3}$$

In reactions where chlorite is the product, the standard potential is –1.160 V and the potential varies according to:



$$E = -1.160 - 0.0591 \log \left\{ \left(p_{\text{ClO}_2} \right) \left[\text{ClO}_2^- \right] \right\} \tag{5}$$

In gaseous reaction systems where HCl gas is formed, the standard potential E° is 1.436 V and the potential varies according to:

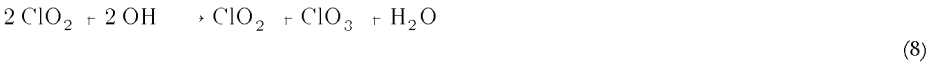


$$E = 1.436 + 0.0591 \text{ pH} - 0.0118 \log \left[\left(p_{\text{ClO}_2} \right) \left(p_{\text{HCl}} \right) \right] \tag{7}$$

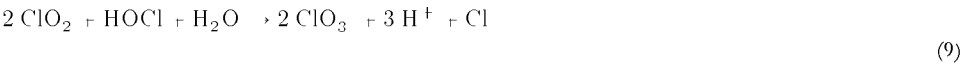
Thermal Decomposition of ClO₂. Chlorine dioxide decomposition in the gas phase is characterized by a slow induction period followed by a rapid autocatalytic phase that may be explosive if the initial concentration is above a partial pressure of 10.1 kPa (76 mm Hg) (27). Mechanistic investigations indicate that the intermediates formed include the unstable chlorine oxide, Cl₂O₃. The presence of water vapor tends to extend the duration of the induction period, presumably by reaction with this intermediate. When water vapor concentration and temperature are both high, the decomposition of chlorine dioxide can proceed smoothly rather than explosively. Apparently under these conditions, all decomposition takes place in the induction period, and water vapor inhibits the autocatalytic phase altogether. The products of chlorine dioxide decomposition in the gas phase include chlorine, oxygen, HCl, HClO₃, and HClO₄. The ratios of products formed during decomposition depend on the concentration of water vapor and temperature (27).

Surface area can accelerate the decomposition of chlorine dioxide up to a point, but sufficient area appears to inhibit catalytic decomposition by adsorption of the intermediates. For example, the presence of fluffed wood pulp or glass wool is reported to stop the explosive decomposition of chlorine dioxide (27).

In solution, chlorine dioxide decomposes very slowly at ambient temperatures in the dark. The primary decomposition process is hydrolysis of chlorine dioxide into chlorite and chlorate ions. The hydrolysis rate is a function of the concentration of hydroxyl ions and temperature, proceeding rapidly at solution pH values above 10:



Decomposition of chlorine dioxide solutions occurs more rapidly in the presence of chlorine and hypochlorite, producing chlorate and HCl (28):



Photochemical Reactions. The photochemistry of chlorine dioxide is complex and has been extensively studied (29–32). In the gas phase, the primary photochemical reaction is the homolytic fission of the chlorine–oxygen bond to form ClO and O. These products then generate secondary products such as chlorine peroxide, ClOO, chlorine, Cl₂, oxygen, O₂, chlorine trioxide [17496-59-2], Cl₂O₃, chlorine hexoxide [12442-63-6], Cl₂O, and other oxychlorine species. In aqueous solutions, chlorine dioxide photolyzes in a complex manner. Chlorate, ClO₃[–], chloride, Cl[–], and hypochlorite, OCl[–], anions are the principal stable products (33–35).

Organic Chemistry. The chemistry and mechanisms of reactions of chlorine dioxide with organic compounds have been extensively reviewed (36–39). A compilation of kinetic data is also available (40). The reactions of chlorine dioxide with organic compounds must be distinguished with regard to the specific reaction conditions. For example, reactions may take place using chlorine dioxide in the gas phase or dissolved in aqueous or nonaqueous solutions. In addition, the reaction pH conditions may be low or high at corresponding reactant and oxidant concentrations. Chlorine dioxide typically reacts with organics as an oxidant with little or no chlorination. The breaking of organic carbon–carbon bonds is generally not extensive in most of the reactions so that the oxidation by-products are also organics. Saturated aliphatic hydrocarbons do not react with aqueous chlorine dioxide, and ClO₂ does not react with carboxylic acids, R–COOH, where R is a saturated alkyl group.

In aqueous solutions, primary and secondary amines react very slowly or not at all with chlorine dioxide (36,41). Chlorine dioxide rapidly oxidizes tertiary amines, producing a secondary amine and an aldehyde. It rapidly oxidizes phenolic compounds, first by oxidation to quinones and eventually by ring opening reactions. However, ClO₂ has a relatively low oxidizing activity toward olefins (37). Alcohols and carbonyl compounds react somewhat more slowly with chlorine dioxide to produce carboxylic acids. Organic sulfides react with chlorine dioxide to form sulfonyl compounds and oxygen-containing products, thus effectively eliminating many odors (37,39). Chlorine dioxide has also been found to react with some chlorinated phenolic compounds, reducing toxicity (39). Partial oxidation of phenol with chlorine dioxide can produce mono- and dichlorinated benzoquinones. But when sufficient chlorine dioxide is used to fully oxidize phenol, the primary products are oxalic and maleic acids as well as carbon dioxide.

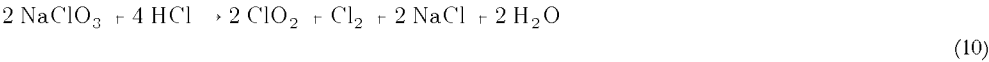
Manufacture

Laboratory Preparation. Pure chlorine dioxide is easily prepared in small quantities by the addition of dilute sulfuric acid into a solution of sodium chlorite (42). A purified air or nitrogen stream passed through a potassium iodide solution or chromium(II) solution is used to sparge the generated ClO₂ gas through a scrubber containing a sodium chlorite solution for the removal of any chlorine contaminants. The gas can then be used directly or absorbed into high purity deionized water. An alternative generation method involves passing a 4–6 vol % mixture of dilute chlorine gas in nitrogen through a dry, packed column of sodium chlorite (43,44). The preparation and solution storage of chlorine dioxide should be done in the absence of uv or strong visible light. The solutions should be kept cold to minimize vapor losses from the solution. Chlorine dioxide easily permeates many polymers, including fluoropolymers.

Small- and Medium-Scale Industrial Production. Sodium chlorite is the preferred raw material for chlorine dioxide production in quantities of less than about 2000 kg d. This is typical for water treatment and disinfection applications. Other applications not requiring high purity, ie, chlorine-free, chlorine dioxide can use chemical generation methods reacting sodium chlorate and hydrochloric acid, sulfuric acid, and mixtures containing sodium chloride. High conversions of chlorate can be achieved by the addition of large excesses of acid and a reducing agent (45). Some of these processes prevent the separation of chlorine dioxide from the highly acidic generator solution by maintaining sufficient pressure.

Large-Scale Industrial Production. Large amounts of chlorine dioxide are used in pulp bleaching and smaller quantities are used for the manufacture of sodium chlorite. In these applications, sodium chlorate is the only commercially available raw material. Chlorine dioxide production from sodium chlorate is achieved by the reduction of the chlorate ion in the presence of strong acid. The reaction consumes acid, so that acid and reducing agents must be constantly added to maintain the reaction.

Chloride Reductant. Processes prior to 1945 used hydrochloric acid as both the acid and reducing agent. Hydrochloric acid is oxidized to chlorine gas and chlorate is reduced to chlorine dioxide. The overall stoichiometry produces a 2:1 molar ratio of chlorine dioxide to chlorine. Sodium chloride is a by-product:



This reaction is not driven to completion unless there is a large excess of HCl; thus the HCl consumption is substantially higher than the stoichiometry would imply.

Sulfuric acid is an economical alternative source of acid and many commercial generators substitute concentrated sulfuric acid for HCl. Furthermore, the required chloride ion needed as the reductant is already present or added as NaCl in the chlorate solution or crystal obtained from the chlorate manufacturer. This process, popular in the 1960s and 1970s, produces substantial amounts of liquid effluent containing 20–35% sulfuric acid, 20–25% sodium sulfate, and minor amounts of sodium chloride and unreacted chlorate that must be neutralized with alkali.

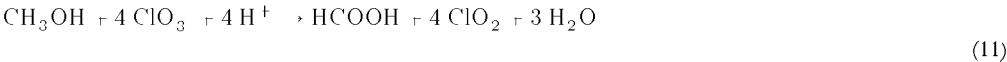
An integrated process for producing chlorine dioxide that can consume chlorine (46) involves the use of hydrochloric acid as the reductant. The spent chlorine dioxide generator liquor is used as feed for chlorate production, and hydrogen gas from chlorate production is burned with chlorine to produce hydrochloric acid. The principal disadvantage in the integrated hydrochloric acid-based processes is that the chlorine dioxide gas contains ¹/₂ mole of chlorine for each mole of chlorine dioxide produced. A partial purification is achieved by absorption in chilled water in which the solubility of chlorine is less than chlorine dioxide; however, this product still contains 10–15% chlorine on the basis of total chlorine and chlorine dioxide.

Sulfur Dioxide Reductant. The Mathieson process uses sulfur dioxide, sodium chlorate, and sulfuric acid to produce chlorine dioxide gas with a much lower chlorine content. The sulfur dioxide gas reductant is oxidized to make sulfuric acid, reducing the overall acid requirement of the process. Air is used to dilute the chlorine dioxide produced by this process. The exit gases flow through a scrubber to which chlorate is added in order to remove any unreacted sulfur dioxide. Spent liquor, containing some unreacted chlorate, sulfuric acid, and sodium sulfate, continuously overflows from this process.

Small amounts of chlorine, amounting from 1 to 5% of the chlorine dioxide, are present in the chlorine dioxide gas product from the Mathieson process. The purity of the chlorine dioxide gas can be increased at the expense of higher chlorate content in the spent liquor if NaCl is not used in the reactor and a small amount of sulfur dioxide gas is present in the generator chlorine dioxide product gas stream.

Various improvements in the sulfur dioxide reduction processes have been commercialized, including the Canadian International Paper Process (1946) and the Kesting, Persson, and Holst processes. A variation combining both chloride and sulfur dioxide reductant processes was developed and patented by KemaNord AB (47).

Organic Reductant Processes. A wide range of organic compounds can be used as reducing agents in the production of chlorine dioxide from sodium chlorate. Carboxylic acids, alcohols, and carbohydrates have been reported as reducing agents, but methanol is the only organic reductant used in commercial generators. Methanol, first used in the Solvay process, is employed in processes licensed by Albright and Wilson Americas and Eka Nobel. These processes use sulfuric acid as the acid source and produce chlorine dioxide containing low levels of chlorine.

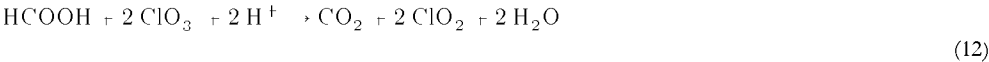


In improved methanol reductant processes, sulfuric acid demand is reduced by crystallizing out by-product sodium sulfate, sodium sesquisulfate, or sodium bisulfate. The particular sodium sulfate salt that is formed depends on the operating temperature and acidity of the generator. The most popular generators use a single vessel operating both as a generator and crystallizer operating under a vacuum. Vacuum operation allows water to evaporate from the generator solution to maintain steady-state concentrations in the generator liquor and to dilute the chlorine dioxide gas.

Chlorine dioxide decomposition occurrences in the generator system are less explosive when operating under reduced pressure with water vapor

present. Generator operation events can sometimes occur, referred to as white-outs, during which production from the generator suddenly stops, and the gas produced contains significant amounts of chlorine.

Chlorine dioxide produced from the methanol reductant processes contains carbon dioxide and small amounts of formic acid. For this reason, sulfur dioxide and chloride-based chlorine dioxide processes are still used for sodium chlorite production. This problem has been addressed by recycling a portion of the vapor from methanol-based generators so that formic acid further reacts to carbon dioxide:



Improvements to the methanol reductant processes may be found in the patent literature. These include methods of operation to reduce acidity in the crystallization zone of the generator to promote crystallization of sodium sulfate and to reduce sulfuric acid consumption (48). Other improvements sought are the elimination of formic acid and chlorine impurities from the chlorine dioxide, as well as methods of recovering acid and sodium hydroxide, or acid and neutral sodium sulfate from the solid sodium sesquisulfate salt waste stream (48–52).

Other Reductants. Sulfur, carbon, and carbon monoxide have been identified as potential reducing agents for chlorate, but no processes using these have been commercialized. Several recent patents describe chlorine dioxide generator processes using hydrogen peroxide [7722-84-1] as a reducing agent in combination with sodium chlorate and acid. Generator operation in an acid normality range of 2–5 *N* produces a neutral sodium sulfate by-product salt (53), whereas a sodium sesquisulfate salt is made operating in a range of 5–11 *N* (54).

Electrochemical Reduction and Catalytic Processes. Electrochemical reduction methods for producing pure chlorine dioxide from acidic solutions containing sodium chlorate have been developed (55–60). At low acidities, chloride ion must be present in order to promote the reduction of chlorate. The need for addition of chloride ion indicates that chlorine dioxide is actually being formed by chloride reduction followed by the electrolytic reduction of chlorine to chloride ion (55). The electrolytic reduction process may be catalyzed using platinum group metal oxide coated cathodes in an acid solution containing sodium chlorate (56). More complex electrochemical processes have been proposed using multiple membrane separated cell compartments to reduce acidified sodium chlorate electrochemically to chlorine dioxide with coproduction of sodium hydroxide (57,58). Electrochemical reduction processes producing chlorine dioxide from chloric acid [7790-93-4], HClO₃, have also been developed. One process uses chloric acid from the ion exchange of sodium chlorate (59). Another reduction process employs chloric acid produced from the thermal or electrochemical oxidation of hypochlorous acid [7790-92-3], HOCl (60). Catalytic methods of producing chlorine dioxide in acid and sodium chlorate solution mixtures using platinum group metal oxide catalysts have also been described (61–63).

Other Significant Process Developments. Increasing chlorine dioxide bleaching substitution levels in the pulp mills, as well as the need for chlorine-free chlorine dioxide, are the driving forces for future process design changes in commercial generator systems using sodium chlorate. The trends in the chlorine dioxide generator systems are being driven toward the reduction or elimination of the sodium sulfate by-product salt cake because of limited recovery boiler capacity in many pulp mills in the United States and Canada. One method of resolving this problem is converting the by-product sodium sulfate salt cake to sulfuric acid and sodium hydroxide by employing electrochemical salt-splitting technology (64,65) (see ELECTROCHEMICAL PROCESSING).

Alternative technology developments are focusing on the use of chloric acid as a generator feed in place of sodium chlorate, thus reducing the requirement for acid addition and minimizing or eliminating salt cake by-product. Methods for the formation or *in situ* production of chloric acid from sodium chlorate by ion exchange (qv) (59), electrodialysis (qv) (66,67), or by integrating an electrochemical cell with a generator (66,68,69) may be found in the literature. Other methods of chloric acid production are by the thermal decomposition or electrochemical oxidation of hypochlorous acid (60,70). In an alternative development, an electrochemical process producing variable composition chloric acid sodium chlorate mixtures from sodium chlorate with the coproduction of sodium hydroxide, has been developed (71). The mixtures can be directly fed into a generator to balance the daily sulfur requirements of individual pulp mills as required.

A process for producing chlorine-free chlorine dioxide, called the O1 PROCESS technology, was announced by Olin Corp. in early 1992 (72). The process uses a pure chloric acid feedstock and proprietary catalysts that utilize water as the reducing agent. The overall reaction chemistry of the process is



The process requires water vapor removal from the generator to be balanced with the water introduced with the chloric acid feed. Significantly greater chlorine dioxide generator capacity is achievable than using the older design generators.

Other ClO₂ Generation Methods. A method of generating chlorine dioxide has been described using a high temperature inert gas plasma reaction using a chlorine and oxygen gas mixture having at least a 2.5:1 molar ratio of oxygen to chlorine (73).

Production and Shipment

In all cases, chlorine dioxide is produced at the point of use either from sodium chlorite or sodium chlorate. Production volume can be accurately estimated from total sodium chlorate consumption for chemical pulp bleaching because this use accounts for greater than 95° of all chlorine dioxide production. The annual North American production of chlorine dioxide since 1970 is given in Table 2.

Table 2. Chlorine Dioxide Production in North America, 10³ t/yr^a

Year	United States	Canada	Total
1970	79	47	126
1975	81	63	144
1980	146 ^b	122	268
1985	226	130	356
1990	361	200	561

^a Ref. 74.

^b Estimated value.

Economic Aspects

The costs of manufacturing chlorine dioxide from sodium chlorate vary for different processes depending on the degree of integration with chlorate manufacture and the need for by-products produced from chlorine dioxide production. The principal costs of chlorine dioxide manufacture are determined by the consumption of sodium chlorate, acid, and reducing agent, together with the fixed costs of operating and maintaining the facility. Estimates in 1992 ranged from \$1100 to \$1800 per metric ton.

The cost of manufacturing chlorine dioxide from sodium chlorite is about two to four times higher than that from sodium chlorate. However, the fixed operating costs of small-scale chlorate-based processes are much higher. The production costs from sodium chlorite are governed by the cost of the chlorite, and the related costs of the handling and storage of the oxidizing agents and or acids used to generate the chlorine dioxide.

Uses

The uses for chlorine dioxide take advantage of the high oxidizing power and broad-spectrum disinfection capability.

Pulp Bleaching. Wood pulp bleaching is the largest use of chlorine dioxide, which is a uniquely selective oxidizer for lignin. Unlike other oxidizing bleaches such as ozone, hydrogen peroxide, oxygen, or chlorine, chlorine dioxide does not attack cellulose and thus preserves the mechanical properties of bleached pulp. Chlorine dioxide bleaching is more effective than other methods at removing incompletely defibered wood or shives (75–78). Compared with other oxidative bleaching chemicals, chlorine dioxide is the most expensive to produce, but it can actually reduce overall bleaching costs under certain conditions (78).

Pulp bleaching is normally performed in several oxidative stages separated by alkaline extraction stages and washing. In final oxidative bleaching stages, chlorine dioxide is the most frequently preferred bleaching chemical. Pulp bleaching practice in the United States makes use of mixtures of chlorine and chlorine dioxide in first-stage bleaching to reduce the formation of organic chlorine compounds in the bleaching process while minimizing total chemical cost (75,77,78).

The formation of chlorinated organic compounds in the pulp is measured as absorbable organic halides (AOX) or as total organically bound chlorine (TOCl). The amount formed during bleaching appears to be a linear function of the chlorine and chlorine dioxide added. Chlorine dioxide contributes about ¹/₅ the chlorinated organic compounds, as does chlorine. However, when individual chlorinated compounds are measured, a more complex, nonlinear relationship is found. Formation of the most toxic highly polychlorinated phenolic compounds, particularly dioxins and chlorofurans, can be eliminated with only partial substitution of chlorine dioxide for chlorine (see CHLOROCARBONS AND CHLOROHYDROCARBONS, TOXIC AROMATICS). As chlorine dioxide is substituted for chlorine, the distribution of chlorinated species shifts from polychlorinated compounds to dichloro and monochlorinated compounds. Even when pure chlorine dioxide is used, some amounts of monochlorinated organics are formed during bleaching (78,79).

The stoichiometric relationship between chlorine dioxide added and color removed during bleaching is nonlinear, but it is independent of temperature, pH, and pulp concentration under conditions normally used. Models used to explain the kinetics and stoichiometry show a strong dependence on chromophore concentration that probably results from differences in the reaction rates of the various chromophores present in the pulps (80).

When chlorine dioxide is used for pulp bleaching in conjunction with the Kraft (sulfide) process for chemical pulping, by-product sodium sulfate can be used as a source of makeup sulfur and sodium consumed in the chemical cycle. The demand for sodium and sulfur in pulp bleaching is related to the loss of these chemicals through carryover in unbleached pulp. As process improvements have sought to reduce pollution from pulp mills, less sodium sulfate makeup is required. The trends in pulp bleaching to increase substitution of chlorine with chlorine dioxide have caused an oversupply of sodium sulfate, so that this by-product is often regarded as waste (81).

Where pressured to provide bleaching alternatives that avoid the use of chlorine containing compounds entirely, pulp producers have developed bleaching processes that use ozone in place of chlorine dioxide. However, when bleaching kraft pulps, ozone must be used in conjunction with oxygen delignification and does not produce pulp having the same combination of brightness and strength as using chlorine dioxide. However, combinations of chlorine dioxide and ozone have demonstrated better bleaching, resulting in less loss of pulp yield and strength than for ozone alone. These processes also demonstrate exceptionally low AOX per metric ton of pulp produced (82–85).

Pulp bleaching with chlorine dioxide is most often performed at an acidic pH, so that the final pH of the bleach liquor is in the range of 2–5. Under these conditions, the residual concentration of chlorite and chlorate ions in the bleach liquor are minimized and chloride ion is the predominant chlorine species in the spent bleach (77). In addition to direct addition to pulp in bleaching, chlorine dioxide also finds use in wastewater treatment from pulp mill operations as a means to remove effluent color (85).

Other Uses. As a biocide, chlorine dioxide is more effective than chlorine over a wider pH range. Chlorine dioxide is also less corrosive and more compatible with some materials of construction. Chlorine dioxide has a wide variety of small applications in drinking water, food processing (qv), cooling towers, and oil recovery. In these areas, chlorite is the preferred source of chlorine dioxide.

Toxicology

Gaseous chlorine dioxide is explosive at concentrations above 10.1 kPa (76 mm Hg) partial pressure (10 vol %) in air. Explosions may be caused by an electrical discharge including static electricity, hot surfaces, metal oxides, or organics, and may be self-initiated after an induction period. Flame propagation velocities for explosive decomposition are a function of the initial partial pressure of chlorine dioxide and range from 1 m s at 16.7 kPa (125 mm Hg), to more than 5 m s at 40 kPa (300 mm Hg) (23,86). Explosions are much more violent and may occur at lower concentrations when organic vapors are present. When involved in a fire, chlorine dioxide is a source of oxygen. The decomposition reactions of chlorine dioxide may produce hazardous by-products such as hydrochloric acid, chlorine, and chloric acid.

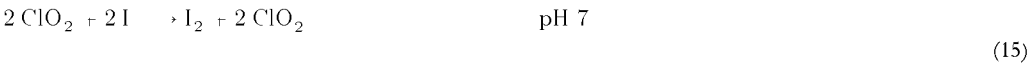
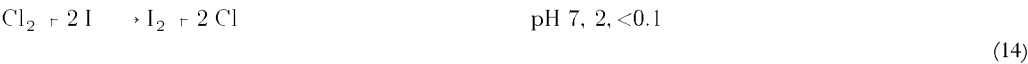
The threshold limit value–time integrated average, TLV–TWA, of chlorine dioxide is 0.1 ppm, and the threshold limit value–short-term exposure limit, STEL, is 0.3 ppm or 0.9 mg m³ of air concentration (87,88). Chlorine dioxide is a severe respiratory and eye irritant. Symptoms of exposure by inhalation include eye and throat irritation, headache, nausea, nasal discharge, coughing, wheezing, bronchitis, and delayed onset of pulmonary edema. Delayed deaths occurred in animals after exposure to 150–200 ppm for less than one hour. Rats repeatedly exposed to 10 ppm died after 10 to 13 days of exposure. Exposure of a worker to 19 ppm for an unspecified time was fatal. The ingested systemic effects of low concentration chlorine dioxide solutions are similar to that of chlorite.

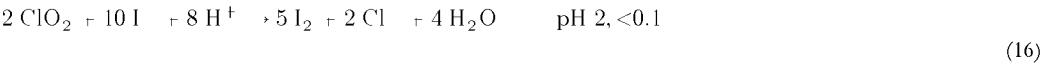
Chlorine dioxide solutions are normally stored cold at concentrations of less than 10 g L in order to keep the concentration of gaseous chlorine dioxide above the aqueous solutions below the explosive limit. Chlorine dioxide solutions are corrosive to the skin and eyes, and solutions must be handled with adequate ventilation to avoid exposure to the gas. Protective equipment required for chlorine dioxide are impervious clothing, neoprene gloves and boots, gas-tight chemical splash goggles and face shields, as well as other appropriate clothing to prevent the possibility of skin contacting aqueous solutions or vapor. Clothing contaminated with chlorine dioxide should be removed immediately and thoroughly washed. In the event of spills or leaks, personnel not wearing appropriate safety equipment should be immediately evacuated from the area. NIOSH MHSA-approved respiratory protection is required for chlorine dioxide concentrations above 0.1 ppm. For ClO₂ concentrations above ~10 or unknown ppm, self-contained breathing apparatus is required for entry and escape and in firefighting. All sources of ignition should be removed and the area of the leak or spill should be ventilated and the source of the leak stopped. Any residual material should be flushed with large quantities of water. Contaminated material and residues should be disposed of in a manner approved for this material. Manufacturer MSDS data sheets and technical information should be consulted (87,88).

Analytical and Test Methods

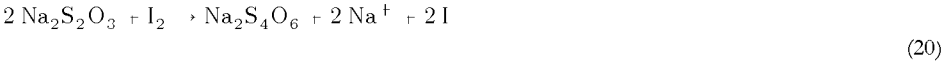
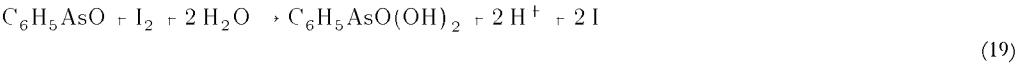
Reagents similar to those used in the analysis of chlorine are commonly employed in the quantitation of gaseous and aqueous chlorine dioxide as well as its reaction coproducts chlorine, chlorite, and chlorate. The volatility of the gas from aqueous solutions as well as its reactivity to light must be considered for accurate analysis. Other interferences that must be taken into account include other oxidizers such as chloramine, hydrogen peroxide, permanganate, and metal impurities such as ferrous and ferric iron.

The iodometric analysis method for ClO₂ and its coproducts is based on the pH-dependant oxidation of potassium iodide to selectively distinguish the various oxychlorine species from each other (42,89). The reactions of the oxidizer species with iodide at various pH buffered conditions are





Use of a pH buffer of 8–9 has been suggested as a substitute for the pH 7 buffer for more accurate analysis. Sodium thiosulfate [10102-17-7], Na₂S₂O₃, or phenylarsine oxide [637-03-6], C₆H₅AsO₃, are the typical titrants.



These titrations can be done manually using a starch indicator for end point detection or more accurately by amperometric methods. Ion chromatography is being qualified as a standard method for chlorite and chlorate analysis (90). Flow injection analysis methods have also been developed based on the iodometric pH adjusted reaction chemistry illustrated in equations 14–18 using spectrophotometric detectors (91,92). A colorimetric method using *N,N*-diethyl-*p*-phenylenediamine [93-05-0] (DPD), C₁₀H₁₁N₂, (42) is popular but is subject to interferences from other oxychlorine oxidizing species present. Colorimetric methods using chlorophenol red [4430-20-0] have been found to be specific for ClO₂ without interferences from chlorine (93,94). A detailed review of the various oxychlorine analytical methods is available (95). Commercially available process analyzers have been developed for the online measurement and control of chlorine dioxide gas and aqueous solution generation systems. A gas chromatography method has been described for measuring Cl₂ and ClO₂ in gases (96). Near uv spectroscopic methods are the most common, suitable for aqueous ClO₂ in the 0.05–10 g/L range and in the ppm to vol % ranges for gaseous ClO₂. Amperometric and oxidation–reduction potential (ORP)-based sensors (qv) are commercially available for ClO₂ solutions and gases in the ppm and mg/L and lower ranges.

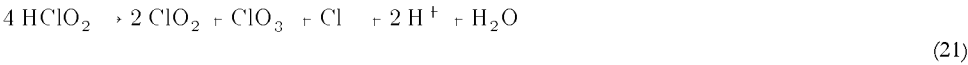
CHLOROUS ACID AND CHLORITES

Physical Properties

Chlorous Acid. The physical properties of HClO₂ have been determined using acidified alkali metal chlorite solutions. The existence of HClO₂ is based on spectroscopic evidence (6,13,97). **Sodium Chlorite.** The Cl–O bond lengths in the chlorite ion are about 0.156 nm and the bond angle is between 108–110° (98–101). The uv absorption spectra of aqueous chlorite solutions have a maximum at about 260 nm. The crystallization of sodium chlorite from aqueous solutions yields solid sodium chlorite trihydrate [49658-21-1], NaClO₂·3H₂O, at temperatures below 37.4°C. Anhydrous NaClO₂ [7758-19-2] forms above 37.4°C. The anhydrous form is not hygroscopic (102,103) and is slightly soluble in methanol. Analytical-grade NaClO₂ (mol wt = 90.442) is a colorless crystalline solid that decomposes as it melts between 180–200°C. Technical-grade (80 wt % assay) NaClO₂ is a white solid that may have a slight greenish tint from trace amounts of ClO₂ or metals such as iron.

Chemical Properties

Chlorous Acid. The chemical properties of HClO₂ have been determined from the acidification of alkali metal chlorites. The *K_a* acid dissociation constant of chlorous acid at 25°C, reported to be about 1.1 × 10^{–2} (104,105), has been measured using rapid scan spectrophotometric methods and determined to be 1.9 × 10^{–2} (106). The standard enthalpy, Gibbs free energy, and standard entropy for HClO₂ at 298.15 K are Δ*H*° = 51.9 kJ/mol (12.4 kcal/mol), Δ*G_f*° = 5.9 kJ/mol (1.4 kcal/mol), and *S*° = 0.1013 kJ/(mol·K) (0.024 kcal/(mol·K)), respectively (107). The overall disproportionation of chlorous acid in acidic solutions in the absence of chloride ion has been reported as:



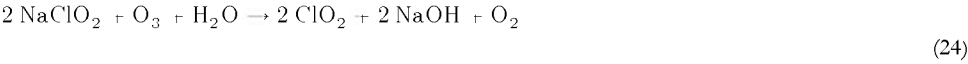
In the presence of added chloride, chlorate ion is formed in negligible amounts.



Equation 22 gives the maximum theoretical obtainable chlorine dioxide from the disproportionation of HClO₂. Experimentally, differences in the stoichiometry have been reported. This is because the chloride formed in equation 21 can catalyze the reaction to form more chlorine dioxide as in equation 22. Proposed mechanisms for these reactions and the kinetics under various conditions have been described (16,108). **Sodium Chlorite.** The standard enthalpy, Gibbs free energy of formation, and standard entropy for aqueous chlorite ions are Δ*H*° = 66.5 kJ/mol (15.9 kcal/mol), Δ*G_f*° = 17.2 kJ/mol (4.1 kcal/mol), and *S*° = 0.1883 kJ/(mol·K) (0.045 kcal/(mol·K)), respectively (107). The thermal decomposition products of NaClO₂ in the 175–200°C temperature range are sodium chlorate and sodium chloride (102,109):



About 5 wt % of the chlorite goes to oxygen. At higher temperatures, the by-product sodium chlorate melts at about 260°C and decomposes above about 448°C. Sodium chlorite is not shock sensitive unless contaminated with organics. Commercial alkaline sodium chlorite solutions are stable so long as light is excluded. Solutions can even be boiled with little assay loss. Hydrogen peroxide reduces chlorite very slowly in a pH range between 3 and 9 (102). Many of the metal chlorites are not particularly stable and will explode or detonate when struck or heated. These include the salts of Hg⁺, Tl⁺, Pb²⁺, Cu⁺, and Ag⁺. Extremely fast decomposition with high heat evolution has been noted for barium chlorite [14674-74-9], Ba(ClO₂)₂, at 190°C, silver chlorite [7783-91-7], AgClO₂, at 120°C, and lead chlorite [13453-57-1], at 103°C (109). Sodium chlorite can be oxidized by ozone to form chlorine dioxide under acidic conditions (110):



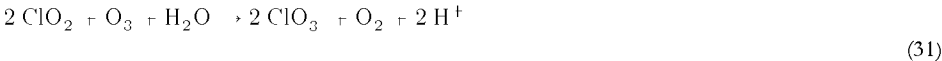
The proposed mechanistic details are (111):



The generated ClO₂ has a competing reaction with excess ozone to form chlorate. Mechanistically,



yielding the net equation:

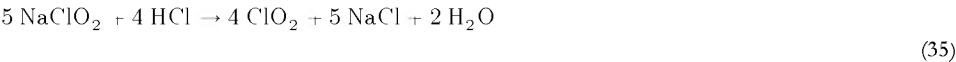


Sodium chlorite is used to produce chlorine dioxide by chemical oxidation, electrochemical oxidation methods, or by acidification with acids. Most of the commercial methods employ chlorine or sodium hypochlorite.

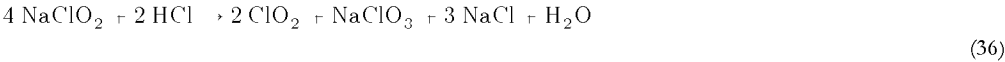
Acid–Sodium Chlorite System. The addition of a strong inorganic acid into an aqueous sodium chlorite solution produces chlorous acid, which rapidly disproportionates into chlorine dioxide. One proposed set of reactions using hydrochloric acid is (110):



yielding the net equation:



A secondary reaction path produces by-product chlorate and has a proposed net reaction of:

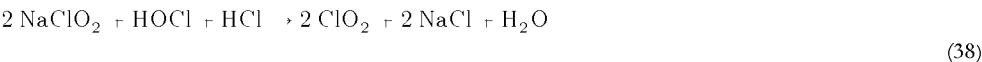


The maximum chlorite to chlorine dioxide theoretical molar yield using HCl is only 80%. In practice, 85–90% of the 80% molar theoretical yield is obtained using a 300% molar excess of strong HCl (112). A patented generator design employs a strong acid stream and a concentrated chlorite solution using a water eductor system to draw off and dilute the high concentration chlorine dioxide gas containing liquid stream (113). Chlorine dioxide yields from chlorite by acidification using sulfuric acid generally does not exceed about 60–70% of the theoretical 80% molar yield. The methods using hydrochloric acid give increased conversion yields because of the presence of chloride ion. The acid–chlorite generating systems are commonly used in very small-scale operations for convenience.

Hypochlorous Acid–Sodium Chlorite System. In this method, chlorine gas is educted into water forming a hypochlorous acid solution which then reacts with aqueous sodium chlorite to produce chlorine dioxide (114–116). Hypochlorous acid, formed from the disproportionation of chlorine gas in water:



reacts with sodium chlorite to produce ClO₂:



Demonstrated chlorine dioxide yields from chlorite are 95% or higher in properly operated systems. Excess hypochlorous acid is commonly used to achieve a high conversion.

Chlorine Gas–Sodium Chlorite System. In this method, chlorine gas reacts directly with a concentrated sodium chlorite solution under a vacuum and chlorine dioxide gas is removed from the reaction chamber using a water-based eductor (117). The reaction has a 100% theoretical molar conversion of chlorite:



Chlorine dioxide yields of 95% or greater have been demonstrated. The use of chlorine as an oxidant has distinct advantages because it is usually present in municipal water treatment plants for water disinfection.

Sodium Hypochlorite–Acid–Sodium Chlorite System. In this method, hydrochloric or sulfuric acid is added into a sodium hypochlorite [7681-52-9], NaOCl, solution before reaction with the sodium chlorite (118).



The acid addition shifts the chlorine solution equilibrium to favor molecular chlorine. The hypochlorous acid–chlorine equilibria is



(41)

The pH of the chlorine dioxide reaction mixture must be maintained in the 2.8–3.2 pH range, otherwise decreased conversion yields of chlorite to chlorine dioxide are obtained with by-product formation of chlorate. Generator efficiencies of 93% and higher have been demonstrated. A disadvantage of this system is the limited storage life of the sodium hypochlorite oxidant solution.

Photochemical Generation of Chlorine Dioxide from Chlorite. Several methods of generating chlorine dioxide by the photochemical oxidation of chlorite have been reported in patents. The chlorite solution is irradiated using a light source and the chlorine dioxide generated is swept from the solution using an inert gas stream. Low concentrations of ClO₂ gas are produced (119,120). In another method, ultraviolet light is used in conjunction with salts or hydrogen ions added to a chlorite solution (121).

Electrochemical Generation of Chlorine Dioxide from Chlorite. The electrochemical oxidation of sodium chlorite is an old, but not well-known method of generating chlorine dioxide. Concentrated aqueous sodium chlorite, with or without added conductive salts, is oxidized at the anode of an electrolytic cell having a porous diaphragm-type separator between the anode and cathode compartments (122–127). The anodic reaction is



The generated chlorine dioxide must be air stripped from the anode compartment in order to achieve high chlorite conversion efficiency. Sodium ions from the anode compartment are transported into the cathode compartment, forming sodium hydroxide [1310-73-2] and hydrogen gas coproducts:



giving a net reaction of:



A concentrated waste stream containing chlorate by-product and residual unreacted chlorite is generated from anodic oxidation of ClO₂ and chlorite side reactions to chlorate. Oxidation-resistant perfluorinated ion-exchange membrane separators (see MEMBRANE TECHNOLOGY) and solid polymer electrolyte electrodes have improved process performance and reduced by-product formation (128–130). An alternative electrochemical process producing aqueous chlorine dioxide and coproduct sodium hydroxide from the *in situ* acid activation of sodium chlorite has been developed (131). New electrochemical generation technology employing high surface area anodes have also been developed, producing chlorine-free aqueous chlorine dioxide solutions from dilute chlorite solutions. Chlorite to chlorine dioxide conversion efficiencies of 95% or better have been demonstrated in a single flow-through pass with no by-product chlorate–chlorite waste streams (132–134).

Mechanisms in Chlorine Dioxide Generation from Chlorite. The reactions between sodium chlorite and chlorine-based oxidizers and acids are complex and involve the formation of the proposed unsymmetrical intermediate, [Cl₂O₂] (16,18,22,36,108,135–140).

The reactions of chlorite and chlorine and or hypochlorous acid are



Mechanistically, equations 45 and 46 involve the formation of a [Cl₂O₂] intermediate:



At high reactant concentrations, this intermediate is favored and rapidly formed. It then decomposes in a second order reaction to form chlorine dioxide and chlorine:



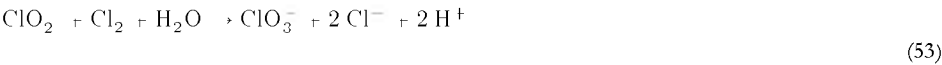
The generated chlorine further reacts with additional chlorite as given in equation 47, so that the net reaction of the intermediate with chlorite can be written as



The reaction chemistry changes when the initial reactant concentrations are low or there is excess hypochlorous acid present. The [Cl₂O₂] intermediate disproportionation route to chlorine dioxide becomes less important (eq. 48), and the route to chlorite formation by hydrolysis predominates as does the reaction with any available excess HOCl to form chlorate and chlorine:



Large amounts of chlorate are formed when there is a large excess of chlorine or HOCl in relation to chlorite. These chlorate forming reactions are



The conditions for chlorate formation are high pH, low reactant concentrations, and the presence of excess chlorine or hypochlorous acid. Thus, the addition of free chlorine or hypochlorite to chlorine dioxide treated water, which contains chlorite as a by-product of the chlorine dioxide treatment, predominantly forms chlorate in the pH 5–8 range typically used in water treatment (140).

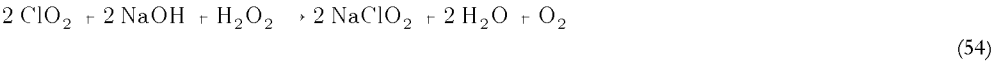
Organic Reactions. The chlorite ion, ClO₂[–], is mostly a weak and slow oxidizer in alkaline aqueous solutions. Aldehydes (qv) can be readily oxidized to the corresponding carboxylic acids in neutral or weakly acidic solutions. Mixing solid sodium chlorite with combustible organic materials can result in explosions and fire on shock, exposure to heat, or flames.

Manufacture

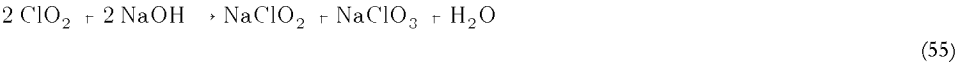
Sodium chlorite is the only chlorite compound produced on a commercial scale. Technical-grade sodium chlorite is an 80 wt % assay solid product containing other added salts, such as sodium chloride, which act as diluents for increased safety in storage and handling. The various sodium chlorite solution grades similarly have varying amounts of other salts.

The commercial manufacture of sodium chlorite is based almost entirely on the reduction of chlorine dioxide gas in a sodium hydroxide solution containing hydrogen peroxide [7722-84-1/ as the reducing agent. The chlorine dioxide is generated from the chemical or electrochemical reduction of sodium chlorate under acidic conditions.

In the general process, chlorine dioxide gas is absorbed into a cooled (15–20°C) circulating solution containing sodium hydroxide and hydrogen peroxide. The predominant reaction is (141,142):



A secondary competing reaction can occur where chlorine dioxide disproportionates in the alkaline solution, producing sodium chlorite and chlorate:



The reaction in equation 55 occurs when there is insufficient hydrogen peroxide reductant in the absorber solution. Monitoring of the hydrogen peroxide concentration is important because H₂O₂ is unstable in strong alkaline solutions, decomposing to water and oxygen. A small excess of sodium hydroxide is maintained to stabilize the final chlorite solution product. The yield of sodium chlorite from the absorbed chlorine dioxide is generally 95% or better. Process methods for controlling the hydroxide peroxide liquid absorber operation using pH and or redox potential for high yield production of chlorite from the raw materials have been described (141–143).

Production and Shipment

Solution sodium chlorite is shipped by producers and distributors in specified plastic containers, plastic drums, tote tanks, isotainers, and tank trucks. Dry product is shipped in 45.36 kg, 50 kg, and 80 kg capacity drums in the United States. Sodium chlorite is not authorized for bulk transport as a solid. Sodium chlorite solutions with more than 5% available chlorine have a U.S. Department of Transportation (DOT) shipping classification as a class 8 corrosive, identification number UN1908, with a group II packaging requirement. Sodium chlorite dry powder or flake is a class 5.1 oxidizer, identification number UN1496, also with a group II packaging requirement. The DOT HM-181 regulations on the containers, packaging, markings, and transportation of sodium chlorite are published in the *Federal Register* under the *Hazardous Materials Regulations* (HMR), covering the transportation of hazardous materials in commerce (144,145). In Canada, the regulations are under the *Transportation of Dangerous Goods Regulations*. The latest issue of the regulations should be consulted for any additions or changes.

Economic Aspects

The specific use applications of sodium chlorite varies from country to country. Important factors are the regulatory and environmental laws in effect for air and water quality standards. Sodium chlorite is generally priced at about four to six times the cost of sodium chlorate. The list price of 80% technical-grade NaClO₂ in January 1991 was \$2.65 /kg (146). In 1990, the estimated consumption of sodium chlorate for the production of sodium chlorite in Canada was about 2700 metric tons and about 9100 metric tons in the United States (74). In Western Europe, the 1990 chlorate consumption estimate was about 11,000 metric tons. A summary of 1991 U.S. and foreign sodium chlorite producer annual plant capacities in various world market areas is given in Table 3.

Table 3. 1991 Sodium Chlorite Production Capacity

Company	Country	Capacity, t ^{a,b}
<i>North America</i>		
Olin Corp. ^c	United States	7700
Albright & Wilson Americas, Inc., ^d Div. of Tenneco Canada Inc.	Canada	4000 ^e
<i>Western Europe</i>		
Energia e Industria Aragonesas, SA	Spain	1500
Atochem SA	France	7000
Degussa AG	Germany	5000
Hoechst AG	Germany	5000
Caffaro SpA	Italy	4000
<i>East Asia</i>		
Kuk-do Chemical Industry Co., Ltd.	South Korea	3000 ^e
Nippon Carlit Co., Ltd.	Japan	2500
Daiso Chemical Co., Ltd.	Japan	1800
Hodogaya Soda Co., Ltd.	Japan	2500
Nippon Soda Co., Ltd.	Japan	1800

^a Ref. 74.

^b Estimated or actual production capacities for 80% assay basis sodium chlorite.

^c Sale of chlorite business unit to Vulcan Chemicals (Birmingham, Ala.) announced in June 1992.

^d Sale of chlorite business to Sterling Chemicals (Houston, Tex.) announced in March 1992.

^e Information from public news releases and or personal communication.

The principal U.S. manufacturers and or water service companies that sold or leased chlorine dioxide generating equipment and services in 1991 were Aquatec, Capital Controls, Chemquip, Drew Chemical (Division of Ashland Chemical), Fischer & Porter, Prominent Fluid Controls, Rio Linda, and Wallace & Tieman.

Specifications, Standards, and Quality Control

Technical-grade solid and solution sodium chlorite for use in potable water treatment has specifications listed by the American Water Works Association (AWWA) (147), the National Sanitization Foundation (NSF), and the American National Standard NSF International (148). In the AWWA specification standards, technical solid sodium chlorite should not contain less than 78.0 wt % NaClO₂. The impurity limits for 80% assay sodium chlorite should not be more than 17.0 wt % sodium chloride, 3.0 wt % sodium carbonate, 3.0 wt % sodium sulfate, and 0.0003 wt % arsenic. The AWWA standards also specify the analysis procedures for all of the chemical components in the sodium chlorite.

Toxicology

The toxic effects of sodium chlorite are directly related to its oxidant properties. Details of toxicological studies are summarized in reviews (149,150). Sodium chlorite is toxic mainly from ingestion. The acute oral LD₅₀ is approximately 180 mg/kg (rat) for the 79 wt % assay product. The dermal LD₅₀ exposure is low, greater than 2 g/kg (rabbit). Sodium chlorite produces severe irritation or burns to the skin or eyes. Corneal damage and impairment of vision may occur if this material is not washed immediately from the eyes. Sodium chlorite is slightly toxic to most fish and other aquatic organisms. For bluegill (*Lepomis macrochirus*) the median tolerance limit, TL₅₀, is 208 mg/L and the lethal concentration fifty, LC₅₀, values are 265–310 mg/L. For rainbow trout (*Salmo gairdneri*), the TL₅₀ is 50.6 mg/L and LC₅₀ is 290 mg/L. Of the aquatic species tested, Daphnia is the most sensitive with an LC₅₀ of 0.29 mg/L (150).

Sodium chlorite is not listed by the USEPA or any regulatory authority as a carcinogen. Studies conducted in mice and rats did not show an increase in tumors in animals exposed to sodium chlorite in their drinking water. Sodium chlorite has been found to have mutagenic activity in some *in vitro* test systems such as the Ames Salmonella reverse mutation assay without the presence of metabolic activators. The significance of these test results in regard to human health is not clear because of the oxidizing effects of the chlorite ion (149).

Controlled animal and human clinical studies on the effects of sodium chlorite and/or chlorine dioxide have been conducted in a 1–1000 mg/L concentration range. Metabolically, both ClO₂ and ClO₂⁻ are rapidly reduced following ingestion. Most of the chlorine is excreted from the urine in the form of Cl⁻ ion with a small amount of ClO₂⁻. The no observed effect level, NOEL, from animal studies involving ClO₂ and ClO₂⁻ generally ranges between 10 and 100 ppm. Exposure of laboratory animals to ClO₂ above 100 mg/L in drinking water have shown a decrease in blood cell glutathione, red blood cell counts, and hemoglobin. Some mild effects on the thyroid and anemia were noted in younger laboratory animals. Human volunteers in one study with doses up to 24 mg/L of ClO₂ or ClO₂⁻ showed no adverse health effects (149).

Dry sodium chlorite decomposes at temperatures above about 175°C, forming sodium chloride, sodium chlorate, and oxygen as by-products. The reaction is extremely exothermic and therefore self-sustaining. Sodium chlorite should be kept away from heat or flames. Contact or mixing of sodium chlorite with acids can produce poisonous and possibly explosive mixtures of chlorine dioxide and chlorine gas. Sodium chlorite is incompatible with all combustibles, reducing agents, and oxidizers. Mixtures or contamination of sodium chlorite with oxidizable, combustible, or organic materials can be easily ignited by heat or friction and may spontaneously burn or explode. Examples of these materials are cloth, wood, paper, greases, oils and solvents, rubber, leather, and plastics. Sodium chlorite is especially incompatible with sulfur, sulfur compounds, powdered metals, and phosphorous and ammonium compounds (150).

Protective personal equipment for handling sodium chlorite includes splash-proof goggles, neoprene gloves and boots, waterproof or washable outer clothing, and a dust mask for powder handling. All chlorite contaminated clothing should be washed quickly and thoroughly with water to prevent fires. Spills should be contained and dampened with water before collecting into clean metal or high density polyethylene containers to reduce fire hazards. Contaminated materials should be washed or incinerated in an environmentally acceptable manner. Material Safety Data Sheets (MSDS) issued by the sodium chlorite manufacturer should be consulted before handling and use.

Uses

More than 80% of all the sodium chlorite produced is used for the generation of chlorine dioxide. Sodium chlorite or the chlorine dioxide generated from it or from sodium chlorate must be registered with the USEPA for each specific application use as a biocide for microbial growth control or disinfection. These regulations are covered under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

Municipal/Industrial Water Treatment. The principal consumption of sodium chlorite is as the precursor in chlorine dioxide generation for use as an effective disinfectant alternative in municipal and wastewater treatment. Chlorine dioxide is used for taste and odor control as well as for iron and manganese removal. An estimated 300–400 utilities in the United States have chlorine dioxide treatment equipment (151). One role for chlorine dioxide is in the control of total trihalomethanes (TTHMs) in potable drinking water to meet the USEPA drinking water regulations under the Safe Drinking Water Act Amendment of 1986. The regulation is a 0.10 mg/L maximum contamination level for water systems serving populations of over 10,000 people. Pilot-plant studies have proven chlorine dioxide useful in oxidizing the organic precursors in the water before the final chlorine residual disinfectant is added for controlling TTHMs (152). The present regulations have a recommendation for limiting the amount of total combined residual oxidant levels of chlorine, chlorine dioxide, chlorite, and chlorate to a 1.0 mg/L maximum for chlorine dioxide treated drinking water (153,154). Methods for the removal/reduction of the ClO₂ and/or ClO₂⁻ residuals in drinking water treatment process are being evaluated using ferrous iron compounds (155), sulfur reducing compounds (155–157), anion exchange (158), and carbon adsorption (159,160) as well as by membrane separation methods. Revised USEPA drinking water regulations covering disinfectants and by-products are expected by 1995.

Sodium chlorite generated ClO₂ is also finding increasing use for microbiological control in industrial cooling systems and towers. It is especially useful in replacing chlorine in industrial ammonia plants because of its nonreactivity with ammonia. In many areas of the United States, chlorine dioxide is beginning to replace chlorine because of the concern for handling chlorine in populated areas.

Food Industry Disinfection. ClO₂ solution generated from sodium chlorite is used in the washing of fruits and vegetables as a fungicide and for flume water disinfection. Chlorine dioxide does not react with the large quantity of ammonia compounds present to form chloramines as does chlorine (see CHLORAMINES AND BROMAMINES; FOOD PROCESSING). Other applications using chlorine dioxide for meat and poultry washing and sanitizing food process equipment have been previously approved, but as of this writing are under review by the United States Federal Drug Administration (USFDA).

Industrial Processes. The use of sodium chlorite as an oxidizer in NO_x and SO_x combustion flue gas scrubber systems has been described (161–163). Sodium chlorite has also been used for treatment and removal of toxic and odorous gases such as hydrogen sulfide and mercaptans. Chlorine dioxide from chlorite is also useful for microbial and slime control in paper mills and alkaline paper machine systems (164,165). The use of sodium chlorite in textile bleaching and stripping is well known. Cotton is not degraded by sodium chlorite because the oxidation reactions are specific for the hemicellulose and lignin components of the fibers.

Disinfectant Formulations and Sterilization. Hundreds of applications covering disinfectant compositions using sodium chlorite have been described in U.S. and foreign patents. Some examples of these are as antimicrobial additives for latexes (166), marine antifouling agents (see COATINGS, MARINE) (167,168), antimildew detergent compositions (169), toothpaste and solution compositions for prevention and treatment of periodontal oral disease (see DENTIFRICES) (170–172), and compositions for the disinfection of contact lenses (qv) (173).

In many patent or literature descriptions, a stabilized chlorine dioxide solution or component is used or described. These stabilized chlorine dioxide solutions are in actuality a near neutral pH solution of sodium chlorite that may contain buffer salts or additives to obtain chlorite stability in the pH 6–10 range. The uv spectra of these solutions is identical to that of sodium chlorite. These pH adjusted chlorite solutions can produce the active chlorine dioxide disinfectant from a number of possible organic or inorganic chemical and microbiological reactions that react, acidify, or catalyze the chlorite ion.

Chlorine dioxide gas generated from chlorite has been used as a chemosterilizing agent substitute for ethylene oxide in medical applications (174,175). Aqueous foam compositions containing chlorine dioxide have also been developed for the sanitization of hard surfaces (176).

Metallurgical and Ore Processing. Sodium chlorite is used in solution formulations to oxidize the copper surfaces in multilayer circuit boards for better adhesion as well as in other electronic applications (177–179). The use of oxidant gases including chlorine dioxide and chlorine generated in an electrochemical cell has been proposed for the desulfurization of coal (see COAL CONVERSION PROCESSES, CLEANING AND DESULFURIZATION) (180). Chlorine dioxide is also described for lowering the viscosity of coal–water slurries by reacting with sulfides in the coal (181). Processes using chlorine dioxide generated from sodium chlorite have also been described for the recovery of precious metals from carbonaceous ores (182) and by ore leaching (183).

Oil Field and Petroleum Processing. Sodium chlorite is finding increasing use as the choice precursor for generating chlorine dioxide for biocidal control in the production of crude oil (see PETROLEUM). The use of water in the oil field pumping and processing systems presents significant

corrosion problems related to the growth of sulfate-reducing bacteria. Chlorine dioxide does not react with most of the aromatic components present in the crude oil and also has the advantage of not forming chlorinated hydrocarbon by-products as in the case of chlorine. Chlorine dioxide also helps in the separation of the crude oil from the water by breaking up emulsions and by reacting with the sulfides and phenolic compounds present (184–190). Sodium chlorite is used in drilling muds as a biocide for protecting the organic additives from degradation (191). In addition, sodium chlorite is used in combination with inorganic acids, such as hydrochloric or sulfuric acid, in generating chlorine dioxide for hydraulic fracturing or restoring the permeability of the underground formations around wellbores by direct injection or stimulation into wells (192–196).

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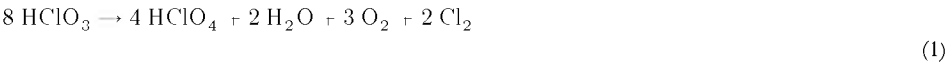
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CHLORIC ACID AND CHLORATES

Chloric Acid

Chlorates are salts of chloric acid [7790-93-4], HClO₃.

Physical Properties. Aqueous chloric acid is a clear, colorless solution stable when cold up to ca 40 wt % (1). Upon heating, chlorine [7782-50-5], Cl₂, and chlorine dioxide [10049-04-4], ClO₂, may evolve. Concentration of chloric acid by evaporation may be carried to >40% under reduced pressure. Decomposition at concentrations in excess of 40% is accompanied by evolution of chlorine and oxygen [7782-44-7] and the formation of perchloric acid [7601-90-3], HOCl₄, in proportions approximating those shown in equation 1.



Impurities such as chloride ion or other reducing agents generate chlorine dioxide when the chloric acid solution is heated. Transition-metal ions do not affect the stability of pure chloric acid at room temperature. Thirty-five percent solutions of HClO₃ have been shown to be stable for 20 days at room temperature containing up to 1000 ppm Ni²⁺, 800 ppm Zn²⁺, 700 ppm Fe³⁺, or 600 ppm Cr³⁺ (2). The solubility of chloric acid in water is shown in Figure 1.

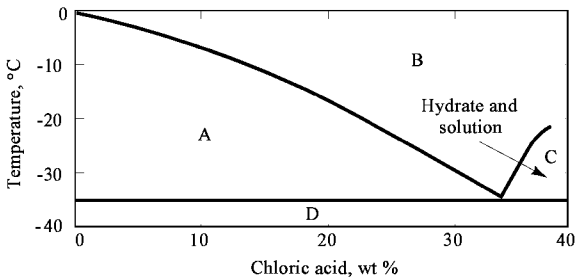


Fig. 1. Solubility of chloric acid in water where A represents ice and chloric acid solution; B, solution; C, chloric acid hydrate and solution; and D, a eutectic of ice and the hydrate (2).

Chloric acid, a strong acid, has pK_a = 2.7 (3). It is a strong oxidizing agent, E₀ = 1.175 V with ClO₂ as the reduction product (4). The heat of formation is -99.2 kJ/mol (-23.7 kcal/mol) and the Gibbs free energy of formation is -3.3 kJ/mol (-0.79 kcal/mol) for both chloric acid and the chlorate ion (4).

Chemical Properties. Chloric acid is a strong acid and an oxidizing agent. It reacts with metal oxides or hydroxides to form chlorate salts, and it is readily reduced to form chlorine dioxide.

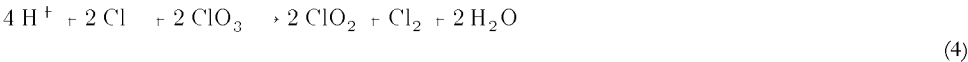


Titanium, Hastelloy (grades C22 and C276), and 316 stainless steel all exhibit corrosion rates of less than 0.08 mm/yr at room temperature in 35 wt % chloric acid solutions (2).

Manufacture. Chloric acid is the precursor for generation of chlorine dioxide for pulp bleaching and other applications (see BLEACHING AGENTS), and is formed *in situ* by reaction of sodium chlorate [7775-09-9], NaClO₃, and a strong acid, eg,



Any chloride present in the solution is oxidized to chlorine by the chloric acid.



In order to eliminate or reduce the sodium sulfate by-product of reaction (3), activity has focused on the direct manufacture of chloric acid.

Emerging technologies for the commercial manufacture of chloric acid fall into three categories: (1) generation of high purity chloric acid by thermal decomposition of pure solutions of hypochlorous acid [7790-92-3], HOCl (5).



The chlorine generated as a by-product is recovered. Stable solutions of up to 40% by weight chloric acid are generated by evaporative concentration. The chloric acid obtained is free of metal cations and chloride and sulfate anions; (2) generation of chloric acid by passing a solution of sodium chlorate through a cation ion-exchange resin (6,7). Electrochemical methods for producing chloric acid from sodium chlorate have also been developed (see ELECTROCHEMICAL PROCESSING). These include electrodialysis (qv) methods employing discrete anion and cation membrane separated compartments or bipolar membranes (8,9) (see MEMBRANE TECHNOLOGY). An alternative electrochemical process employs perfluorinated cation-exchange membrane bounded cell compartments to produce high concentration chloric acid–sodium chlorate mixtures. The mixture is evaporated under vacuum to crystallize out sodium chlorate and produce a low sodium content chloric acid (10). All of the electrochemical routes to chloric acid produce sodium hydroxide, oxygen, and hydrogen as coproducts. The resulting HClO₃ solution contains some dissolved sodium chlorate as well as the impurities that were present in the initial sodium chlorate solution; (3) and hypochlorous acid can be oxidatively electrolyzed to chloric acid (11,12). Chloric acid prepared by oxidizing HOCl is both metal- and chloride-ion free. It can be reduced to chlorine dioxide without the formation of solid by-products or chlorine. This reduction can be conducted electrochemically (7,13,14) or chemically (13,14).

Uses. Chloric acid is formed *in situ* by reaction of sodium chlorate and a strong acid during chlorine dioxide production. Stoichiometric amounts

of sodium salts are also formed as a by-product. The use of chlorine dioxide for pulp (qv) bleaching applications is growing and disposal of the by-product solids is a primary environmental concern. Use of chloric acid to generate chlorine dioxide can eliminate this problem.

Chloric acid also has found limited applications as a catalyst for the polymerization of acrylonitrile (qv) [107-13-1], C₃H₃N, (15–19), and in the oxidation of cyclohexanone [108-94-1], C H₁₀O (20) (see CYCLOHEXANOL AND CYCLOHEXANONE).

Shipment. Solutions of greater than 10 wt % chloric acid may be shipped using the label, "oxidizing substance, liquid, corrosive, n.o.s.," and using identification number UN3098, packing group II.

Health and Safety Factors. Chloric acid is a strong oxidizing agent and concentrated solutions ignite cedar shavings or dry paper (qv) products (2). The acid must be stored apart from reducing agents and organic materials. Concentrated solutions are corrosive to the skin (1).

Sodium and Potassium Chlorate

Physical Properties. The physical properties of sodium chlorate [7775-09-9] and potassium chlorate [3811-04-9], KClO₃, are summarized in Table 1 (21). The solubilities of these chlorates in water are given in Figure 2 (22–26).

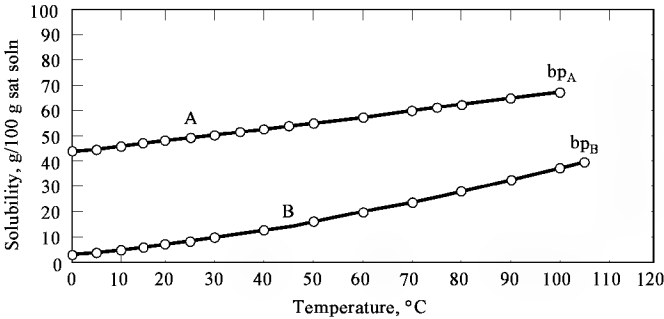


Fig. 2. Aqueous solubility of A, sodium chlorate and B, potassium chlorate where bp_A represents 122°C, the boiling point of a saturated solution of sodium chlorate is 122°C; bp_B represents the boiling point, 104°C, of potassium chlorate solution.

Table 1. Physical Properties of Sodium and Potassium Chlorates

Properties	NaClO ₃	KClO ₃
molecular weight	106.44	122.55
crystal system	cubic	monoclinic
mp, °C	248–260	356–368
dec pt, °C	265	400
density, g mL	2.487 ^a	2.338 ^b
n_D^{20}	1.515	1.440
affinity towards water	hygroscopic	nonhygroscopic
enthalpy of fusion, ΔH_{fus} , kJ mol ^c	21.3	
molar heat capacity, J (molK) ^c	100 ^{b,d}	99.8 ^b
standard enthalpy of formation, kJ mol ^c		
crystals	365.8	391
ideal soln of unit activity	344.1	
standard entropy J (molK) ^c crystals		143
ideal solution of unit activity	22.3	
enthalpy of dissolution, ^e kJ mol ^c	21.6	40.9

^a At 25°C
^b At 20°C
^c To convert J to cal, divide by 4.184.
^d From 298 to 533 K.
^e 1 mol of chlorate per 200 mol H₂O at 25°C.

The electrical conductivity of a pure aqueous sodium chlorate solution is given in Table 2. Additional data are given (27). Table 3 summarizes the solubility data for two aqueous chlorate–chloride systems (28–30).

Table 2. Electrical Conductivity of Aqueous Sodium Chlorate Solutions (ohm·m–1

Concentration, g L	Temperature		
	20°C	40°C	60°C
100	6.2	8.9	11.8
200	10.4	14.9	19.7
300	13.4	18.9	25.0
400	15.0	21.5	28.5
500	15.7	22.7	30.3
600	15.5	23.1	30.8
750		21.7	29.7

Table 3. Mass Ratio of Crystalline Chloride and Chlorate Salts in Equilibrium with an Aqueous Solution

Temperature, °C	Solution system, kg kg of water ^a			
	NaCl	NaClO ₃	KCl	KClO ₃
9.8	0.270	0.360	0.2466	0.0056
10	0.249	0.499	0.3123	0.0144
30	0.2125	0.706	0.3703	0.0321
50	0.1785	0.958	0.4226	0.0635
70	0.1495	1.238	0.4651	0.1162
100	0.1245	1.85	0.518	0.2588

^a Densities of the NaClO₃–NaCl and KClO₃–KCl aqueous solutions are given in Ref. 31.

Chemical Properties. On thermal decomposition, both sodium and potassium chlorate salts produce the corresponding perchlorate, salt, and oxygen (32). Mixtures of potassium chlorate and metal oxide catalysts, especially manganese dioxide [1313-13-9], MnO₂, are employed as a laboratory source of oxygen. The evolution of oxygen starts at ~70°C and becomes rapid at 100°C, below the fusion point (33). The molten chlorates are powerful oxidizing agents. Mixtures of chlorates and organic materials have been employed as explosives. However, because of extreme shock sensitivity and unpredictability, such mixtures are not classed as permissible explosives in the United States. Chlorates also form flammable and explosive mixtures with phosphorus, ammonium compounds, some metal compounds, and some metal salts (34). Chlorates in neutral and alkaline solutions at room temperature do not show oxidizing properties. Concentrated acidic solutions of chlorates are strong oxidants as a result of chloric acid formation and may also liberate chlorine dioxide gas.

Manufacture. Most chlorate is manufactured by the electrolysis of sodium chloride solution in electrochemical cells without diaphragms. Potassium chloride can be electrolyzed for the direct production of potassium chlorate (35,36), but because sodium chloride is so much more soluble (see Fig. 2), the production of the sodium salt is generally preferred. Potassium chlorate may be obtained from the sodium chlorate by a metathesis reaction with potassium chloride (37).

The sodium chlorate manufacturing process can be divided into six steps: (1) brine treatment; (2) electrolysis; (3) crystallization and salt recovery; (4) chromium removal; (5) hydrogen purification and collection; and (6) electrical distribution. These steps are outlined in Figure 3.

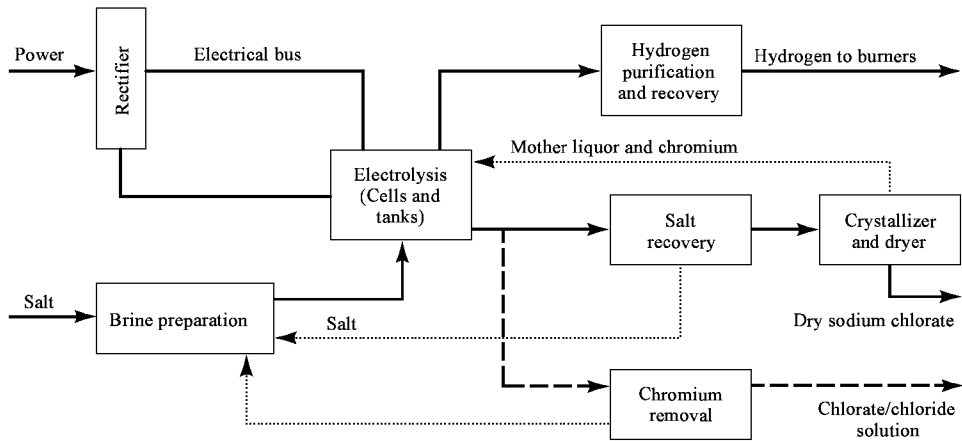


Fig. 3. Schematic of the key steps in a sodium chlorate plant where (···) represents recycle streams and (—), process for solution product. Most plants produce crystalline product.

The production of sodium chlorate is very energy intensive requiring between 4950–6050 kWh of electricity per metric ton of sodium chlorate produced (38). More than 95% of the energy is used in the electrolysis step. Increases in energy cost have resulted in use of highly efficient noble metal coated titanium anodes and elimination of the less efficient graphite anodes (39). The by-product hydrogen generated from the cell is also recovered for its fuel value. Advances in electrical bus connection design have also been incorporated to reduce the cell-to-cell voltage drop. The use of noble metal anodes requires that hardness, ie, Ca²⁺ and Mg²⁺ ions, and metals be removed from the sodium chloride brine, hence the brine treatment technology that was originally developed for chlor-alkali industry has now become an integral part of sodium chlorate manufacture (see ALKALI AND CHLORINE PRODUCTS). Sodium chlorate manufacturing technology now incorporates a low chloride–chlorate solution manufacture coupled with a chromium removal system, or the use of a crystallizer to produce crystal chlorate as the final project.

Electrolysis. The overall chemical reaction is



The reaction in equation 6 requires six Faradays to produce one mole of chlorate. The reaction is endothermic, $\Delta H = 224 \text{ kcal/mol}$ (53.5 kcal/mol) of chlorate or 2.43 kWh/kg. In practice, it takes about 5 kWh of energy to produce a kilogram of sodium chlorate. The remaining energy is lost to electrolyte solution resistance and heat.

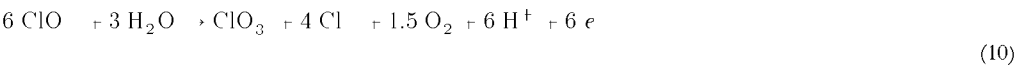
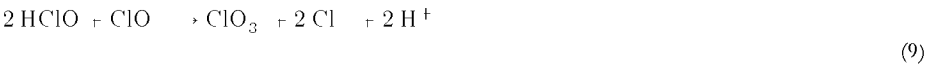
In the sodium chlorate cell, free chlorine is formed at the anode:



The E_0 at 25°C is 1.36 V vs a normal hydrogen electrode (NHE). The chlorine reacts in the boundary layer and hydrolyzes to form HOCl and HCl



which reacts in the bulk electrolyte to form chlorate (40). Hypochlorous acid, HClO, or hypochlorite ions can be converted to chlorate by two separate simultaneous reactions: by the decomposition of hypochlorite ion and free hypochlorous acid (eq. 9) (41) and by the electrochemical formation of chlorate by the anodic oxidation of hypochlorite (eq. 10).



The reaction described in equation 9 occurs at 100% current efficiency; current efficiency of that in equation 10 is only 66.7% (42,43).

The most favorable conditions for equation 9 are temperature from 60–75°C and pH 5.8–7.0. The optimum pH depends on temperature. This reaction is quite slow and takes place in the bulk electrolyte rather than at or near the anode surface (44–46). Usually 2–5 g/L of sodium dichromate is added to the electrolysis solution. The dichromate forms a protective Cr₂O₃ film or diaphragm on the cathode surface, creating an adverse potential gradient that prevents the reduction of OCl⁻ to Cl⁻ ion (44). Dichromate also serves as a buffering agent, which tends to stabilize the pH of the solution (45,46). Chromate also suppresses corrosion of steel cathodes and inhibits O₂ evolution at the anode (47–51).

There are other parallel electrochemical reactions that can occur at the electrodes within the cell, lowering the overall efficiency for ClO₃⁻ formation. Oxygen evolution accounts for about 1–3% loss in the current efficiency on noble metal-based electrodes in the pH range 5.5–6.5.



Where *E*₀ at 25°C is 1.23 V vs NHE at pH = 0, and 0.876 V vs NHE at pH = 6. Oxidation of chlorates to perchlorate can also occur if the cell voltage increases above 6.5 V, or if the chloride concentration is depleted below about 80 g/L.



In addition to the electrochemical reactions, there are some undesirable nonelectrolytic reactions that produce chlorine and oxygen gases, thus lowering the current efficiency (18). Oxygen generated from decomposition of hypochlorite species in bulk accounts for about half of the oxygen involved. The decomposition of the hypochlorite species is catalyzed by low levels of ionic metal impurities, specifically Ni²⁺, Co²⁺, Ir³⁺, and Ir⁴⁺. The current efficiency in the chlorate cell can be monitored by analyzing the exit gas stream and can be calculated by using the following formula:

$$\text{chlorate efficiency} = (100 - 3 W_{\text{O}} - 2 W_{\text{Cl}}) / (100 - W_{\text{O}} - W_{\text{Cl}})$$

(13)

where *W*_O = vol % of oxygen in exit gas and *W*_{Cl} = vol % of chlorine in the exit gas. The approximate energy consumption *P* in (kWh)/t of a chlorate cell is a function of current efficiency CE expressed as a fraction and cell voltage *V* in volts

$$\frac{1509V}{CE}$$

(14)

Current efficiency depends on operating characteristics, eg, pH, temperature, and cell design, and is generally in the 90–98% range. The cell voltage is a function of electrode characteristics and electrolyte conductivity and can be expressed as

$$V = V_{\text{thermo}} + V_{\text{anode}} + V_{\text{cathode}} + V_{\text{ohmic}}$$

(thermodynamic decomposition voltage of the anode and the cathode)
+ (anode overvoltage) + (cathode overvoltage) + (ohmic drop
between the anode and cathode resulting from the electrolyte + gas
mixture) + (ohmic drop in the electrical connections and hardware)

Typical energy requirement and operating condition are summarized in Table 4.

Electrolyzer System. The basic criteria for electrolyzer system design is to minimize capital and operating costs. There are about a dozen electrolyzer system configurations being used for sodium chlorate manufacture. These combinations range from high capital/low operating cost to low capital/high operating cost (53–90). Electrolyzer systems have four basic components: an electrolysis zone, a reaction zone, a cooling zone, and a circulation zone.

In the electrolysis zone, the electrochemical reactions take place. Two basic electrode configurations are used: (1) monopolar cells where the same cell voltage is applied to all anode/cathode combinations; and (2) bipolar cells where the same current passes through all electrodes (Fig. 4). To minimize the anodic oxidation of OCl⁻, the solution must be quickly moved out of this zone to a reaction zone. Because the reaction to convert OCl⁻ to ClO₃⁻ (eq. 9) is slow, a relatively large volume reaction zone is required to carry out the reaction. Moreover, because the energy supplied to the cell is about twice the energy required to carry out the reaction, a cooling zone is required. Then, a circulation zone and circulation mechanism are provided.

Table 4. Electrical Energy Requirement for a Chlorate Cell Using Steel Cathodes and Pt–Ir Anodes^a

current density, kA/m ²	2–3	
current efficiency, %	94	
cell voltage components, V		
thermodynamic decomposition	1.71	
anode overvoltage	0.05	
cathode overvoltage	0.94	
ohmic drops ^b	0.80	
average cell voltage, V		3–3.50
electrical energy requirement, kWh/t ^c	5700	
operating conditions		
temperature, °C	80	
solution composition, g/L		
NaCl	150	
NaOCl	3–5	
NaClO ₃	450	
Na ₂ Cr ₂ O ₇	2–5	

^a Ref. 52.

^b The gap is from 3 to 5 mm.

^c Per metric ton of chlorate formed.

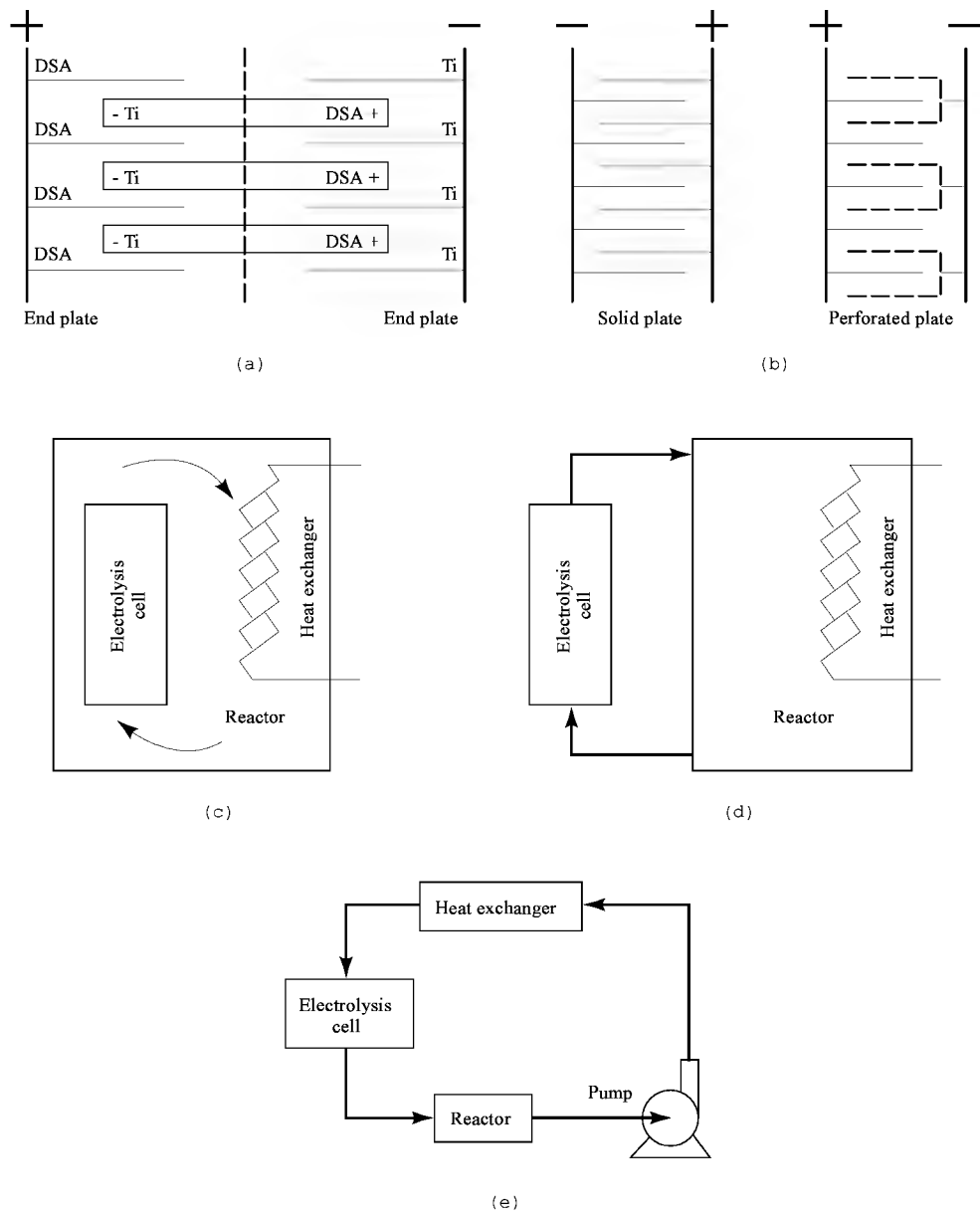


Fig. 4. Sodium chlorate cell designs (a) the horizontal bipolar cells used by Huron having narrow gap vertical plates or horizontal mesh where () represents an insulating partition, DSA is dimensionally stabilized anode, and (b) the parallel plate monopolar cells and electrolyzer configurations used by Chemetics, Krebs, etc where () represents a perforated plate; (c) the single vessel system used by DeNora, Huron, and OCC; (d) the double vessel system used by Krebs; and (e) the three vessel system used by Pennwalt, Ugine-Kuhlmann, and Kemanord. Materials of construction given in Table 5.

Many combinations of these component zones have been designed. Some are shown in Figure 4. The combinations range from all zones in one vessel to vessels for each zone. Materials of construction for the different parts of the electrolyzer system are summarized in Table 5.

Table 5. Materials of Construction for Chlorate Cells^a

Company	Cathode ^b	Cell body	Cell cover	Reactor
Canoxy Squamish	steel	titanium support cradle only for electrodes	FRP	titanium-lined FRP
Chemetric Solvay	steel	PVC-lined FRP, Teflon-lined fiber glass and steel, titanium		PCV-lined FRP, titanium Teflon-lined FRP
Chemwest	titanium	Teflon-lined FRP	Teflon-lined FRP	titanium
DeNora	titanium ^c	Teflon-lined steel	rubber as explosion hatch	Teflon-lined
Eltech	titanium	Teflon-lined FRP	Teflon-lined FRP	Teflon-lined FRP
Huron	titanium	PVC	titanium or Siliglas ^d FRP	titanium or Siliglas ^d FRP
Kemanord	steel	rubber-lined steel	rubber-lined steel	rubber-lined steel
Krebs	steel	steel, with titanium anode cover plate	titanium inlet and outlet reducer connections	titanium
Krebakosmo	steel	frames of PVDF	end plates of steel	titanium
OCC	steel	steel bottom, titanium top	titanium	titanium
Oulu	steel	steel	steel	titanium
Pennwalt	steel	steel	titanium	titanium
Ugine-Kuhlmann	steel	steel bottom, titanium top	rubber as explosion hatch	titanium

^a FRP = Fiber reinforced plastics.

^b Anode material used for anode technologies is coated titanium.

^c Ti 0.2% Pd alloy.

^d Siliglas is patented by Huron.

Brine Preparation. Rock salt and solar salt (see CHEMICALS FROM BRINE) can be used for preparing sodium chloride solution for electrolysis. These salts contain Ca, Mg, and other impurities that must be removed prior to electrolysis. Otherwise these impurities are deposited on electrodes and increase the energy requirements. The raw brine can be treated by addition of sodium carbonate and hydroxide to reduce calcium and magnesium levels to below 10 ppm. If further reduction in hardness is required, an ion-exchange resin can be used. A typical brine specification for the Huron chlorate cell design is given in Table 6.

Table 6. Brine Specification for Huron Sodium Chlorate Cell^a

Component	Maximum concentration, ppm	
Mn	0.01	
Ni	0.01	
Fe	1.0	
Al	1.0	
Ba	0.1	
Zn	0.01	
F	1.0	
cyanide	0.1	
total organics	3.0	
hardness as Ca	4.0 ^b	
Na ₂ SO ₄	25.0 ^c	
NaCl	200 to 315 ^{c,d}	

^a Temperature is a maximum of 75°C.
^b For mild steel cathodes maximum hardness is 2 ppm. Some brines contain up to 20 ppm.
^c Units are g L.
^d Value varies depending on application.

Hydrogen Purification and Recovery. Because the operation of the modern chlorate cell is quite efficient, ie, CE = 90–98%, the hydrogen generated from the cell is quite pure and can be recovered for its fuel value. The hydrogen typically contains 2–3% chlorine and less than 2% oxygen by volume. If the cells are operated at lower than a normal pH of from 5.8–6.4, Cl₂ concentration in the hydrogen can be higher. The chlor-alkali industry has developed an extensive hydrogen recovery technology, which has been transferred to chlorate technology. Typically the hydrogen recovery system includes a caustic scrubber to remove chlorine and a compressor or blower to send hydrogen gas to a fuel burner or boiler (91).

Chlorate Recovery and Salt Removal. Prior to chlorate recovery, the residual hypochlorite in the electrolyzer liquor is destroyed by adding a reducing agent such as formate or urea (91,92). The liquor that contains sodium chlorate, chloride, sulfate, and dichromate is filtered to remove any insoluble particles. The liquor is concentrated by evaporation and sodium chloride is precipitated, filtered, and recycled back to the cell. The liquor is then cooled to yield sodium chlorate crystals, which are separated by centrifugation. The chromium containing centrate is returned to the evaporator or cell feed. Since the feed brine contains sodium sulfate, the sodium sulfate can be removed from the system by purging a small amount of filtrate from the crystallizer (93–96). Alternatively, the sodium sulfate from the filtrate can be crystallized out by the method described in reference 97. Recent advances in chlorine dioxide generation technology require that the sodium chloride content be less than 5% of the solution of sodium chlorate concentration. Sodium chlorate recovered by crystallization will meet this requirement.

Chromium Removal System. Chlorate manufacturers must remove chromium from the chlorate solution as a result of environmental regulations. During crystallization of sodium chlorate, essentially all of the sodium dichromate is recycled back to the electrolyzer. Alternatively, hexavalent chromium, Cr⁶⁺, can be reduced and coprecipitated in an agitated reactor using a choice of reducing agents, eg, sodium sulfide, sulfite, thiosulfate, hydrosulfite, hydrazine, etc. The product is chromium(III) oxide [1333-82-0], Cr₂O₃ (98–106). Ion exchange and solvent extraction techniques have also been utilized for recycling chromium (107–109). The resulting precipitate is easily filtered using ceramic or Teflon filters without the use of precoats so that the filtered chromium oxide can be returned directly to the chlorate process without further treatment. Once in the chlorate cell, the chromium reoxidizes immediately to hexavalent sodium dichromate. Essentially no chromium ever leaves the system (110). Chromium levels of less than 1 ppm are achieved in the final chlorate product.

Chlorate Analysis. Chlorate ion concentration is determined by reaction with a reducing agent. Ferrous sulfate is preferred for quality control (111), but other reagents, such as arsenious acid, stannous chloride, and potassium iodide, have also been used (112). When ferrous sulfate is used, a measured excess of the reagent is added to a strong hydrochloric acid solution of the chlorate for reduction, after which the excess ferrous sulfate is titrated with an oxidant, usually potassium permanganate or potassium dichromate.

Product Specification. Sodium chlorate can be shipped either as solid crystals or preblended chlorate–chloride solution. A typical specification for technical-grade sodium chlorate is NaClO₃, 99.5 wt % min; NaCl, 0.12 wt % max; moisture, 0.20 wt % max; and 5 ppm chromium.

The crystalline sodium chlorate is usually dried in rotary driers to less than 0.2 wt % moisture content and is loaded into shipping containers or stored in moisture-free bins or silos prior to packaging. For conventional chlorine dioxide generators, sodium chlorate is shipped as a solution containing: ca 200 g L (15 wt %, 3.4 M) sodium chloride; ca 350 g L (26 wt %, 3.3 M) sodium chlorate; and 130 ppm chromium. Alternatively, for newer chlorine dioxide generators, 600 g L sodium chlorate; 30 g L sodium chloride; and less than 30 ppm chromium is used.

Economic Aspects. Sodium chlorate production has grown at about a 5% rate since the early 1970s and is expected to grow at 8–10% through 1995. The projected rapid growth is related to the increased use of chlorine dioxide in the pulp and paper industry. The 1991 production capacities of various North American plants are given in Table 7. The price of sodium chlorate has increased from \$165 t in 1970 to about \$480 t in 1991 (113,114).

Table 7. Sodium Chlorate Producers and 1991 Capacities, 10³ t

U.S. Producer	Location	Capacity	Canadian producer	Location	Capacity
American Pacific ^a	Cedar City, Utah	6	Albchem	Bruderheim, Alta.	25
Atochem	Portland, Oreg.	22	Albright & Wilson	Buckingham, Que.	128
Atochem	Tacoma, Wash.	22	Albright & Wilson	N. Vancouver, B.C.	77
Brunswick Chemical ^a	Brunswick, Ga.	195	Albright & Wilson	Thunderbay, Ont.	52
Eka Nobel	Columbus, Miss.	135	BC Chemical	Prince George, B.C.	50
Eka Nobel	Moses Lake, Wash.	45	Canadian Oxy	Amherstburg, Ont.	45
Georgia Gulf	Plaquemine, La.	29	Canadian Oxy	Brandon, Man.	86
Huron Technology ^a	Riegelwood, N.C.	38	Canadian Oxy	Bruderheim, Alta.	50
Huron Technology ^a	Clairborne, Ala.	41	Canadian Oxy	Nanaimo, B.C.	16
Kerr McGee	Hamilton, Miss.	135	Canadian Oxy	Squamish, B.C.	14
Kerr McGee ^a	Henderson, Nev.	12	Eka Nobel	Magoa, Que.	123

Occidental Chemical	Taft, La.	55	Eka Nobel	Valleyfield, Que.	110
			Saskatoon Chem. ^a	Saskatoon, Sask.	45
			St. Anne Chem. ^a	Nackawick, N.B.	10
			Stanchem (PPG)	Beauharnois, Que.	41
<i>Total United States</i>		<i>630</i>	<i>Total Canada</i>		<i>872</i>

^a Captive use.

The production and supply of sodium chlorate in Western Europe and Japan are given in Table 8. The bulk price for sodium chlorate in Western Europe in 1990 was \$0.45 /kg.

Table 8. 1989 Production and Consumption of Sodium Chlorate, 10³ t

Region	Consumption	Production
	<i>European community</i>	
Belgium	11.7	
Denmark	1.4	
France	69	65
Germany	14.4	
Greece	0.0	
Ireland	0.1	
Italy	16.7	15
The Netherlands	0.1	10
Portugal	22.2	15
Spain	34.1	26
United Kingdom	3.5	
	<i>Others</i>	
Austria	9.7	2
Finland	156.8	155
Norway	4.5	5
Sweden	109.7	155
Switzerland	1.2	1
<i>Total Europe</i>	<i>421</i>	<i>449</i>
Japan	51.1	59

Safety and Toxicity. Sodium chlorate is harmful if swallowed, inhaled, or absorbed through the skin. Symptoms of inhalation include burning sensation, coughing, wheezing, and laryngitis. Symptoms of ingestion include nausea, vomiting, abdominal pain, cyanasis, and diarrhea (115–117). Acute oral toxicity in laboratory animals for different species are in 1200–1800 mg/kg range. Lethal doses for children are 2 g and for adults are from 15 to 30 g (200–400 mg/kg). Permissible exposure limit for total dust is 15 mg/m³ and for respirator protection, 5 mg/m³.

Chlorates are strong oxidizing agents. Dry materials, such as cloth, leather, or paper, contaminated with chlorate may be ignited easily by heat or friction. Extreme care must be taken to ensure that chlorates do not come in contact with heat, organic materials, phosphorus, ammonium compounds, sulfur compounds, oils, greases or waxes, powdered metals, paint, metal salts (especially copper), and solvents. Chlorates should be stored separately from all flammable materials in a cool, dry, fireproof building.

Flammable resistant clothing such as Nomex should be worn when working with chlorates. Clothing splashed with chlorate solution should be removed before it dries. Shoes and gloves should be rubberized. Leather (qv) should not be worn. Goggles, face shields, and dust respirators should be worn when necessary to protect against dust, splashing, or spillage. Workers should bathe before leaving the working area.

Sodium chlorate does not burn if exposed to fire, but it decomposes to give off oxygen. Consequently only water is effective in the event of a spill or fire. Water cools and dilutes the sodium chlorate. Carbon dioxide, Halon, dry chemical or dry powder types of fire extinguishers are ineffective. EPA classifies sodium chlorate waste as D001 (ignitable waste). The Clean Water Act lists sodium chlorate as a hazardous substance, which if discharged into or upon water, may require immediate response to mitigate danger to public health and welfare. Hazard ratings for sodium chlorate according to the National Fire Protection Association (NFPA) are shown in Table 9.

Table 9. Hazard Ratings for Sodium Chlorate

Situation	Nonfire ^a	Fire ^a
health (blue)	1	0
flammability	0	0
reactivity	2	2
other	oxy	oxy

^a 4 = extreme, 3 = high, 2 = moderate, 1 = slight, and 0 = insignificant.

Uses. The primary (95%) use of sodium chlorate is in the production of chlorine dioxide for bleaching in the pulp (qv) and paper industry (qv). Uses are summarized in Table 10.

Table 10. North American Uses of Sodium Chlorate, 10³ t/yr

Use	1983	1987	1990
chemical pulp bleaching ^a	513	644	921 ^b
perchlorates and sodium chlorite manufacture	25	27	30
uranium production	17	12	9
agricultural herbicide	6	8	7
other	4	2	0

^a Manufacture of chlorine dioxide.

^b Represents 95% of total consumption.

Chemical wood (qv) pulp bleached with chlorine dioxide has superior brightness over pulps bleached using other reagents (see BLEACHING AGENTS). The strength of the cellulose (qv) fiber is not degraded; thus a whiter and stronger paper is obtained using chlorine dioxide. When chlorine dioxide is used in place of chlorine for bleaching pulp, the adsorbable organic halides (AOX), which include dioxins, are reduced by as much as 90% . However, chlorine dioxide cannot be shipped and is therefore generated by the pulp producers at the bleaching plant.

The second most important (3%) use of sodium chlorate in 1990 was as an intermediate in the production of other chlorates and of perchlorates.

The use of sodium chlorate as in agricultural application amounted to about 7000 metric tons in 1990. The agricultural use of sodium chlorate is as a herbicide, as a defoliant for cotton (qv). Magnesium chlorate is used as a desiccant for soybeans to remove the leaves prior to mechanical picking (see DESICCANTS).

About 9000 metric tons of sodium chlorate were used for uranium production during 1990 in North America. This usage was expected to decline sharply. Minor uses of sodium chlorate include the preparation of certain dyes and the processing of textiles (qv) and furs.

Potassium chlorate is used mainly in the manufacture of matches (qv) and pharmaceutical preparation. In pyrotechnics, chlorate salts may be mixed with certain organic compounds such as lactose to give a relatively cool flame, so that certain dyes may be incorporated in the mixture to give colored flares.

Other Chlorates

Barium chlorate monohydrate [10294-38-9], Ba(ClO₃)₂·H₂O, has colorless monoclinic crystals; mp or loss of water at 120°C; sp gr, 3.18; *n*_D²⁰, 1.562; is prepared by the reaction of barium chloride [10361-37-2], BaCl₂, and sodium chlorate in solution. Barium chlorate precipitates on cooling and is purified by recrystallizing. It is used in pyrotechnics.

Lithium chlorate [13453-71-9], LiClO₃, has rhombic needles; mp 124–129°C; decomposes on heating to 270°C. It is one of the most soluble salts known and it is very hygroscopic. LiClO₃ is prepared by adding lithium chloride [7447-41-8] to sodium chlorate solution. Sodium chloride precipitates, the liquor is concentrated, and the lithium chlorate is filtered and dried. It has limited use in pyrotechnics.

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CHLORITES.

See CHLORINE OXYGEN ACIDS AND SALTS.

CHLORITES (MINERALS).

See SILICA.

CHLOROCARBONS AND CHLOROHYDROCARBONS

Survey,
Methyl chloride,
Methylene chloride,
Chloroform,
Carbon tetrachloride,
Ethyl chloride,
Other chloroethanes,
Dichloroethylenes,
Trichloroethylene,
Tetrachloroethylene,
Allyl chloride,
Chloroprene,
Chlorinated paraffins,
Chlorinated benzenes,
Ring-chlorinated toluenes,
Benzyl chloride,
Toxic aromatics,

SURVEY

Chlorination of various hydrocarbon feedstocks produces many useful chlorinated solvents, intermediates, and chemical products. The chlorinated derivatives provide a primary method of upgrading the value of industrial chlorine. The principal chlorinated hydrocarbons produced industrially include chloromethane (methyl chloride), dichloromethane (methylene chloride), trichloromethane (chloroform), tetrachloromethane (carbon tetrachloride), chloroethene (vinyl chloride monomer, VCM), 1,1-dichloroethene (vinylidene chloride), 1,1,2-trichloroethene (trichloroethylene), 1,1,2,2-tetrachloroethene (perchloroethylene), mono- and dichlorobenzenes, 1,1,1-trichloroethane (methyl chloroform), 1,1,2-trichloroethane, and 1,2-dichloroethane (ethylene dichloride [540-59-0], EDC).

In earlier editions of the *Encyclopedia* there have been articles covering the properties, manufacture, capacities, etc, of polychlorinated biphenyls (PCBs), chlorinated naphthalenes, benzene hexachloride, and chlorinated derivatives of cyclopentadiene. These materials are no longer in commercial use because of their toxicity. However, they still impact on the chemical industry because of residual environmental problems. Their toxicity and environmental impact are discussed (see CHLOROCARBONS AND CHLOROHYDROCARBONS, TOXIC AROMATICS).

Ninety-six percent of the EDC produced in the United States is converted to vinyl chloride for the production of poly(vinyl chloride) (PVC) (1) (see VINYL POLYMERS). Chloroform and carbon tetrachloride are used as chemical intermediates in the manufacture of chlorofluorocarbons (CFCs). Methylene chloride, 1,1,1-trichloroethane, trichloroethylene, and tetrachloroethylene have wide and varied use as solvents. Methyl chloride is used almost exclusively for the manufacture of silicone. Vinylidene chloride is chiefly used to produce poly(vinylidene chloride) copolymers used in household food wraps (see VINYLIDENE CHLORIDE AND POLY(VINYLIDENE CHLORIDE)). Chlorobenzenes are important chemical intermediates with end use applications including disinfectants, thermoplastics, and room deodorants.

U.S. demand for some of the more important chlorinated hydrocarbon derivatives is listed in Table 1 (2,3). Chlorinated solvents (methylene chloride, methyl chloroform, trichloroethylene, and perchloroethylene) have wide ranging applications including use in adhesives, aerosols, extraction solvents, industrial cleaning solvents, paint and coating solvents, and pharmaceuticals. They are also used in dry cleaning, vapor degreasing, metal cleaning, textile processing, and as reaction media. The largest single solvent application, metal cleaning, consumed in excess of 270,000 metric tons of chlorinated solvents in 1990 (4). The use of perchloroethylene in dry cleaning is the second largest solvent application. Methylene chloride is used primarily in paint stripping and aerosol applications. 1,1,1-Trichloroethane has wide use in applications that range from metal cleaning to adhesives, coatings, and aerosols. U.S. demand for the four solvents in 1987 was 872,000 metric tons (see Table 1).

Table 1. U.S. Demand for Chlorinated Hydrocarbons, 10³ t

Compounds	CAS Registry number	1987	1989	1992 ^a	1995 ^a
vinyl chloride	[75-01-4]	3957		4889	
vinylidene chloride	[75-35-4]	68		79	
1,2-dichloroethane	[540-59-0]	7146		8468	
methyl chloride	[74-87-3]	240	272		309
methylene chloride	[75-09-2]	234	214		213
chloroform	[67-66-3]	210	262		266
carbon tetrachloride	[56-23-5]	305	313		159
1,1,1-trichloroethane	[71-55-6]	315	338	315	267
trichloroethylene	[79-01-6]	109	108		104
perchloroethylene	[127-18-4]	214	218		218
chlorobenzene	[108-90-7]	112			
<i>o</i> -dichlorobenzene	[95-50-1]	23			
<i>p</i> -dichlorobenzene	[106-46-7]	47			

^a Projected (2,3).

Environmental Considerations

The use of chlorinated solvents is predicted to decline by the year 2000 as a result of concerns related to smog, groundwater contamination, toxicity, and ozone depletion (5). The Montreal Protocol calls for a phase out for emissive uses of carbon tetrachloride by the year 2000 because of its depletion of stratospheric ozone. Methyl chloroform is also under pressure because its ozone depletion potential (ODP) is approximately 15% of carbon tetrachloride. In spite of methyl chloroform being one of the least toxic solvents that does not contribute to smog, methyl chloroform production is frozen at 1989 levels and will begin a phase out schedule in 1993 that will end production by 2002.

Trichloroethylene use has declined as a result of environmental concerns. However, trichloroethylene may replace some 1,1,1-trichloroethane applications. Perchloroethylene used in small businesses for dry cleaning will be regulated for emissions under the same guidelines as those that govern the large chemical producers. This will cause replacement of perchloroethylene for those applications where recovery is uneconomical. Methylene chloride has been classified as a suspected carcinogen and its use will decline in aerosol and paint stripping applications because of health concerns.

Manufacture

Acetylene has found use as a feedstock for production of chlorinated solvents by reaction with hydrogen chloride or chlorine (6). However, because of safety concerns and the lower price of other feedstock hydrocarbons, very little acetylene is used to produce chlorinated hydrocarbons in the United States (see ACETYLENE DERIVED CHEMICALS).

1,2-Dichloroethane, an important intermediate for vinyl chloride production, is produced by catalytic chlorination of ethylene in either vapor or liquid phase or by oxychlorination of ethylene. Thermal dehydrochlorination of 1,2-dichloroethane produces vinyl chloride and coproduct hydrogen chloride. Hydrogen chloride is commonly recycled to an oxychlorination unit to produce 1,2-dichloroethane or is processed into sales-grade anhydrous or aqueous hydrogen chloride.

Dehydrochlorination of 1,1,2-trichloroethane [25323-89-1] produces vinylidene chloride (1,1-dichloroethylene). Addition of hydrogen chloride to vinylidene chloride in the presence of a Lewis acid, such as ferric chloride, generates 1,1,1-trichloroethane. Thermal chlorination of 1,2-dichloroethane is one route to commercial production of trichloroethylene and tetrachloroethylene.

Some chlorinated methanes are made by the direct thermal chlorination of methane (7). Hydrochlorination of methanol with hydrogen chloride produces methyl chloride (8). Methyl chloride is generally used as feedstock to yield more highly chlorinated methanes, such as methylene chloride and chloroform. Chlorination of benzene in the presence of a catalyst such as ferric chloride, or oxychlorination with hydrogen chloride, yields primarily monochlorobenzene. Additional chlorination gives the dichloro isomers and some higher analogues. Typical manufacturing processes for C₁ and C₂ chlorohydrocarbons are shown in Figure 1. More detailed manufacturing information is given in the articles on the individual compounds.

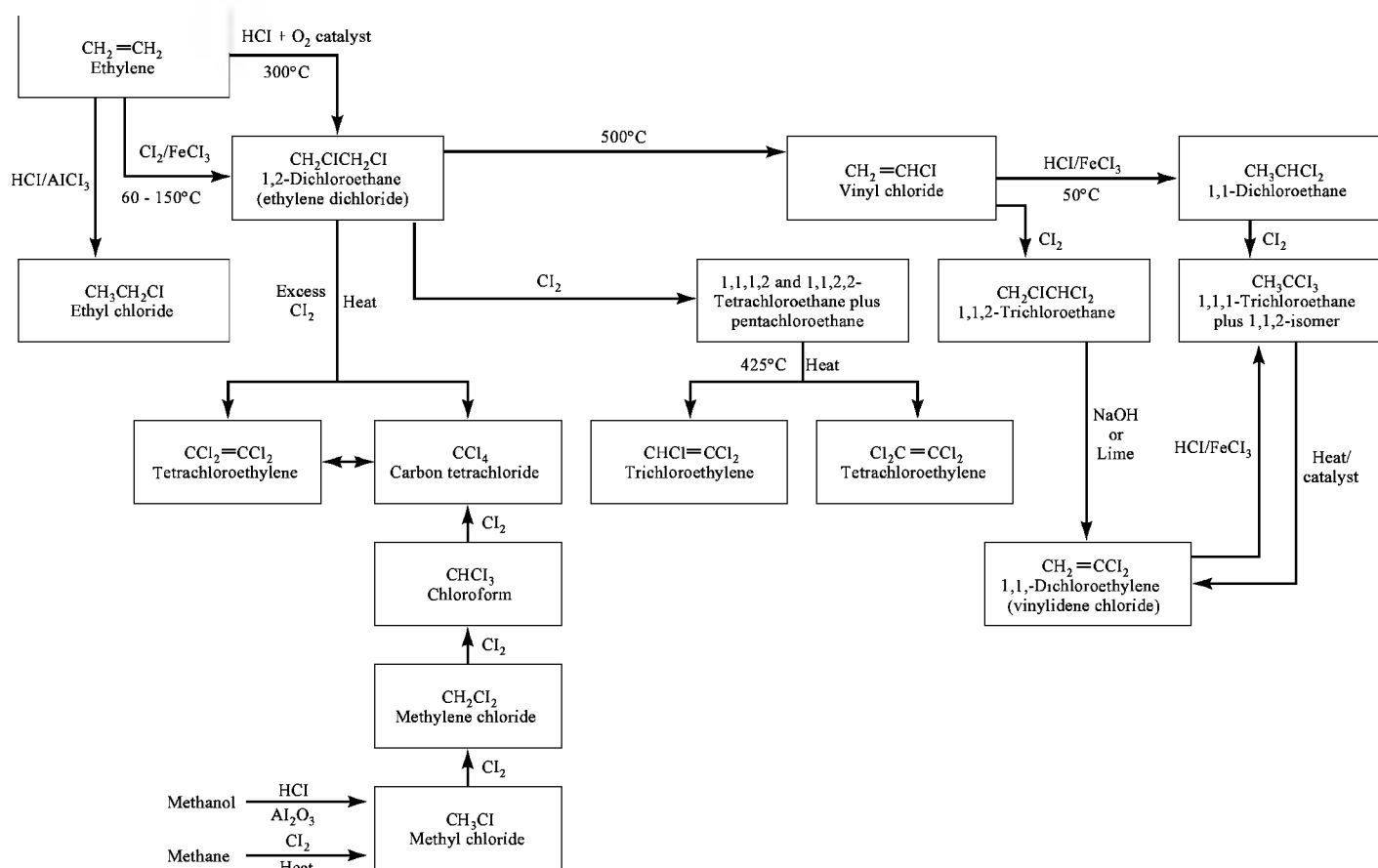


Fig. 1. Manufacturing processes for C₁ and C₂ chlorohydrocarbons.

General Properties of Chlorinated Hydrocarbons

Progressive chlorination of a hydrocarbon molecule yields a succession of liquids and or solids of increasing nonflammability, density, and viscosity, as well as improved solubility for a large number of inorganic and organic materials. Other physical properties such as specific heat, dielectric constant, and water solubility decrease with increasing chlorine content.

All chlorinated hydrocarbons are susceptible to pyrolysis at high temperatures, which liberates hydrogen chloride. Chlorinated alkenes such as trichloroethylene are oxidized in the presence of oxygen when subjected to ultraviolet light or heat to yield hydrogen chloride, phosgene, and chlorinated acetyl chlorides (acid derivatives) (9). Vinylidene chloride polymerizes to a solid very quickly if exposed to air without the presence of a proper inhibitor. Saturated aliphatic chlorine derivatives are usually quite stable to oxidation, although 1,1,2-trichloroethane exhibits appreciable oxidation when contrasted with the stable 1,1,1-trichloroethane isomer. The oxidation of chlorinated hydrocarbons usually proceeds via a hydroperoxide mechanism. Alcohols and amines are often added to oxidation-sensitive solvents to minimize this mode of degradation.

Many chlorinated hydrocarbons react readily with aluminum in the so-called bleeding reaction. A red aluminum chloride-chlorinated hydrocarbon complex is formed. Storage of uninhibited chlorinated solvents in aluminum vessels results in corrosion in a short period of time. Proprietary organic inhibitors permit commercial use of reactive solvents such as 1,1,1-trichloroethane and trichloroethylene for cleaning of aluminum.

Commercial use of many chlorinated derivatives imposes stress on the stability of the solvent. Inhibitors classified as antioxidants (qv), acid acceptors, and metal stabilizers are added to minimize these stresses. All the chlorinated derivatives hydrolyze at a slow but finite rate when dissolved in water. Hydrolysis of chlorinated solvents typically liberates hydrogen chloride that can corrode storage containers and commercial metal-cleaning equipment. The liberated hydrogen chloride can be neutralized by an appropriate epoxide to form noncorrosive chlorohydrins (qv).

All volatile organic solvents are toxic to some degree. Excessive vapor inhalation of the volatile chlorinated solvents, and the central nervous system depression that results, is the greatest hazard for industrial use of these solvents. Proper protective equipment and operating procedures permit safe use of solvents such as methylene chloride, 1,1,1-trichloroethane, trichloroethylene, and tetrachloroethylene in both cold and hot metal-cleaning operations. The toxicity of a solvent cannot be predicted from its chlorine content or chemical structure. For example, 1,1,1-trichloroethane is one of the least toxic metal-cleaning solvents and has a recommended threshold limit value (TLV) of 350 ppm. However, the 1,1,2-trichloroethane isomer is one of the more toxic chlorinated hydrocarbons, with a TLV of only 10 ppm.

Aliphatic Chlorination Reactions

Substitution Chlorination. The substitution of chlorine for hydrogen atoms in a hydrocarbon is an important commercial chlorination process. The chlorination of pentane by the Sharples Solvent Corp. in 1929 has been cited as the first commercial substitution chlorination process in the industry (10). The Chemische Fabrik Griesheim Electron in Germany began production of carbon tetrachloride from methane in the late 1920s, carrying out the reaction over pumice at 500°C. They also pioneered the chlorinolysis reaction for making carbon tetrachloride and tetrachloroethylene, the so-called per-*tet* process. Since chlorine addition to a double bond is much easier than the substitution chlorination reaction of methane and its homologues, the chlorination of unsaturated and aromatic hydrocarbons had been an established industrial process long before the substitution process was developed.

Chlorine free radicals used for the substitution reaction are obtained by either thermal, photochemical, or chemical means. The thermal method requires temperatures of at least 250°C to initiate decomposition of the diatomic chlorine molecules into chlorine radicals. The large reaction exotherm demands close temperature control by cooling or dilution, although adiabatic reactors with an appropriate diluent are commonly used in industrial processes. Thermal chlorination is inexpensive and less sensitive to inhibition than the photochemical process. Mercury arc lamps are the usual source of ultraviolet light for photochemical processes furnishing wavelengths from 300–500 nm.

Chemical initiation generates organic radicals, usually by decomposition of azo (11) or peroxide compounds (12), to form radicals which then react with chlorine to initiate the radical-chain chlorination reaction (see INITIATORS). Chlorination of methane yields all four possible chlorinated derivatives: methyl chloride, methylene chloride, chloroform, and carbon tetrachloride (13). The reaction proceeds by a radical-chain mechanism, as shown in equations 1 through 8.*Chain initiation*



Chain propagation



Chain termination



Chlorine atoms obtained from the dissociation of chlorine molecules by thermal, photochemical, or chemically initiated processes react with a methane molecule to form hydrogen chloride and a methyl-free radical. The methyl radical reacts with an undissociated chlorine molecule to give methyl chloride and a new chlorine radical necessary to continue the reaction. Other more highly chlorinated products are formed in a similar manner. Chain termination may proceed by way of several of the examples cited in equations 6, 7, and 8. The initial radical-producing catalytic process is inhibited by oxygen to an extent that only a few ppm of oxygen can drastically decrease the reaction rate. In some commercial processes, small amounts of air are deliberately added to inhibit chlorination beyond the monochloro stage.

Methane, chlorine, and recycled chloromethanes are fed to a tubular reactor at a reactor temperature of 490–530°C to yield all four chlorinated methane derivatives (14). Similarly, chlorination of ethane produces ethyl chloride and higher chlorinated ethanes. The process is employed commercially to produce 1,1,1-trichloroethane. 1,1,1-Trichloroethane is also produced via chlorination of 1,1-dichloroethane with 1,1,2-trichloroethane as a coproduct (15). Hexachlorocyclopentadiene is formed by a complex series of chlorination, cyclization, and dechlorination reactions. First, substitutive chlorination of pentanes is carried out by either photochemical or thermal methods to give a product with 6–7 atoms of chlorine per mole of pentane. The polychloropentane product mixed with excess chlorine is then passed through a porous bed of Fuller's earth or silica at 350–500°C to give hexachlorocyclopentadiene. Cyclopentadiene is another possible feedstock for the production of hexachlorocyclopentadiene.

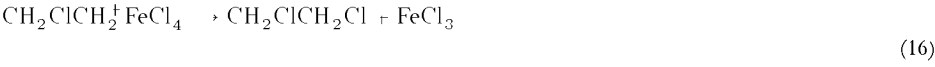
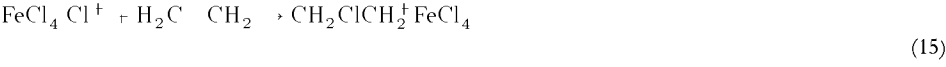
Addition Chlorination. Chlorination of olefins such as ethylene, by the addition of chlorine, is a commercially important process and can be carried out either as a catalytic vapor- or liquid-phase process (16). The reaction is influenced by light, the walls of the reactor vessel, and inhibitors such as oxygen, and proceeds by a radical-chain mechanism. Ionic addition mechanisms can be maximized and accelerated by the use of a Lewis acid such as ferric chloride, aluminum chloride, antimony pentachloride, or cupric chloride. A typical commercial process for the preparation of 1,2-dichloroethane is the chlorination of ethylene at 40–50°C in the presence of ferric chloride (17). The introduction of 5% air to the chlorine feed prevents unwanted substitution chlorination of the 1,2-dichloroethane to generate by-product 1,1,2-trichloroethane. The addition of chlorine to tetrachloroethylene using photochemical conditions has been investigated (18). This chlorination, which is strongly inhibited by oxygen, probably proceeds by a radical-chain mechanism as shown in equations 9–13.



or

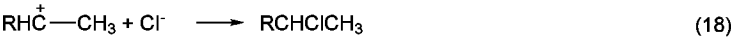
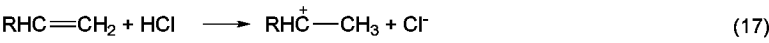


The chlorination of ethylene with a ferric chloride catalyst may be a polar reaction, as shown by equations 14–16 (19).



Hydrochlorination. The addition of hydrogen chloride to alkenes in the absence of peroxides takes place by an electrophilic substitution mechanism. The orientation is in accord with Markovnikov's rule in which the hydrogen atom adds to the side of the double bond that will result in the

most stable carbonium ion. The addition occurs in two steps with formation of an intermediate carbonium ion, as shown in equation 17. Addition of the chloride ion (eq. 18) completes the hydrochlorination mechanism. Metal chloride catalysts are normally used in commercial processes for the hydrochlorination of olefinic derivatives. For example, hydrochlorination of ethylene at temperatures lower than 100°C and in the presence of aluminum chloride yields ethyl chloride. A commercial process for the preparation of 1,1-dichloroethane employs the addition of hydrogen chloride to vinyl chloride in the liquid phase at 50°C in the presence of ferric chloride.



The hydrochlorination of olefins is a weakly exothermic reaction with heats of reaction ranging from 4 to 21 kJ mol (1–5 kcal mol). The hydrochlorination of acetylene is more exothermic, 184 kJ mol (44 kcal mol).

Dehydrochlorination. The primary method for commercially producing vinyl chloride is thermal dehydrochlorination of 1,2-dichloroethane. The gas-phase thermal dehydrochlorination of 1,2-dichloroethane at 350–515°C proceeds by a radical-chain mechanism (20). The reaction is accelerated by radical initiators such as chlorine and retarded or inhibited by olefins and alcohols (21). A typical cracking furnace for the production of vinyl chloride involves a residence time of 3–10 s. The reactor products, on a molar basis, contain an average of 39% vinyl chloride, 39% hydrogen chloride, 22% unconverted 1,2-dichloroethane, and trace amounts of various by-products. The use of activated carbon impregnated with barium chloride permits the cracking operation to proceed at temperatures in the range of 200–350°C. Most vinyl chloride produced by industry is made by thermal, noncatalytic cracking of 1,2-dichloroethane.

Dehydrochlorination of chlorinated derivatives such as 1,1,2-trichloroethane may be carried out with a variety of catalytic materials, including Lewis acids such as aluminum chloride. Refluxing 1,1,2-trichlorethane with aqueous calcium hydroxide or sodium hydroxide produces 1,1-dichloroethylene in good yields (22), although other bases such as magnesium hydroxide have been reported (23). Dehydrochlorination of the 1,1,1-trichloroethane isomer with catalytic amounts of a Lewis acid also yields 1,1-dichloroethylene. Other methods to dehydrochlorinate 1,1,1-trichloroethane include thermal dehydrochlorination (24) and by gas-phase reaction over an alumina catalyst or silica catalyst (25).

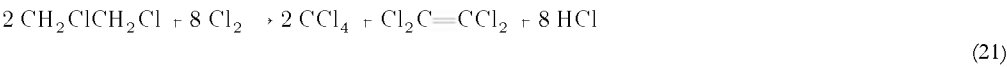
Dehydrochlorination of 1,1,2-trichloroethane at 500°C in the presence of a copper catalyst gives a different product, ie, *cis*- and *trans*-1,2-dichloroethylene. Addition of small amounts of a chlorinating agent, such as chlorine, promotes radical dehydrochlorination in the gas phase through a disproportionation mechanism that results in loss of hydrogen chloride and formation of a double bond. The dehydrochlorination of 1,2-dichloroethane in the presence of chlorine, as shown in equations 19 and 20, is a typical example.



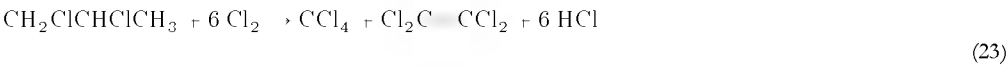
Chlorinolysis. Reaction of C₂ (26) and C₃ (27) hydrocarbons with excess chlorine at high temperatures can cleave the C–C bonds of the hydrocarbon to give chlorinated derivatives of shorter-chain length. A well-known commercial process involving this technique is thermal chlorination of propane and chlorinated hydrocarbon feedstocks with chlorine to produce carbon tetrachloride and tetrachloroethylene with hydrogen chloride as by-product (28). The hydrocarbon feedstock may include hydrocarbons up to C₃ and any partially chlorinated derivatives (29). The yields can be varied widely by controlling recycle streams to take advantage of the equilibrium conversion of carbon tetrachloride to tetrachloroethylene; eg, recycling carbon tetrachloride increases the tetrachloroethylene yield.

A typical reactor operates at 600–900°C with no catalyst and a residence time of 10–12 s. It produces a 92–93% yield of carbon tetrachloride and tetrachloroethylene, based on the chlorine input. The principal steps in the process include: (1) chlorination of the hydrocarbon; (2) quenching of reactor effluents; (3) separation of hydrogen chloride and chlorine; (4) recycling of chlorine to the reactor; and (5) distillation to separate reaction products from the hydrogen chloride by-product. Advantages of this process include the use of cheap raw materials, flexibility of the ratios of carbon tetrachloride and tetrachloroethylene produced, and utilization of waste chlorinated residues that are used as a feedstock to the reactor. The hydrogen chloride by-product can be recycled to an oxychlorination unit (30) or sold as anhydrous or aqueous hydrogen chloride.

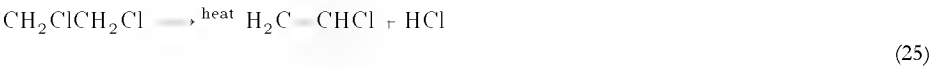
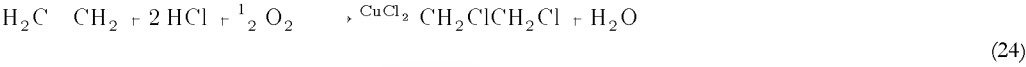
Typical reactions using either 1,2-dichloroethane or 1,2-dichloropropane to produce carbon tetrachloride and tetrachloroethylene by the chlorinolysis reaction are shown in equations 21–23. Continued removal of tetrachloroethylene and recycling of carbon tetrachloride can result in a net zero production of carbon tetrachloride. Most chemical producers using chlorinolysis for the production of perchloroethylene in the future will take advantage of the per tet equilibrium to maximize perchloroethylene to avoid carbon tetrachloride production.*From 1,2-dichloroethane:*



From 1,2-dichloropropane:



Oxychlorination. This is an important process for the production of 1,2-dichloroethane which is mainly produced as an intermediate for the production of vinyl chloride. The reaction consists of combining hydrogen chloride, ethylene, and oxygen (air) in the presence of a cupric chloride catalyst to produce 1,2-dichloroethane (eq. 24). The hydrogen chloride produced from thermal dehydrochlorination of 1,2-dichloroethane to produce vinyl chloride (eq. 25) is usually recycled back to the oxychlorination reactor. The oxychlorination process has been reviewed (31).



Raschig developed the first commercial oxychlorination process in 1928 to make chlorobenzene which was then hydrolyzed to phenol. The Durez plant in North Tonawanda, New York, put on-stream in 1937, used this process.

The first large-scale commercial oxychlorination process for vinyl chloride was put on-stream in 1958 by The Dow Chemical Company. This plant, employing a fixed-tube reactor containing a catalyst of cupric chloride on an active carrier, produced 1,2-dichloroethane from ethylene. The high temperatures involved in the reaction were moderated by a suitable diluent. The average heat output from the reaction is 116 kJ mol (50,000 Btu lb mol).

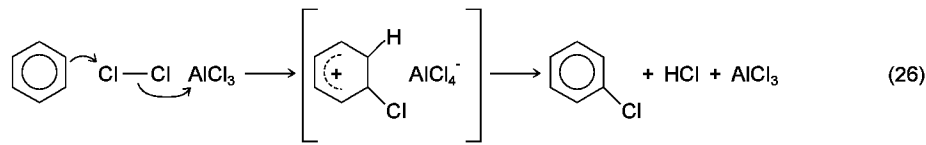
In a typical oxychlorination reaction, preheated gas streams at temperatures of 180–200°C are fed onto a fixed- or fluidized-catalyst bed containing 2–10% copper impregnated on an activated alumina. The reaction occurs during a 15–22 s residence time on the catalyst bed at a temperature of 230–315°C. Typical yields to 1,2-dichloroethane range from 92–97%.

Feeding 1,2-dichloroethane, hydrogen chloride, and oxygen onto a fluidized bed at 400°C produces trichloroethylene and tetrachloroethylene. The catalyst bed consists of cupric chloride and potassium chloride on graphite. A modified oxychlorination technique known as the Transcat process has been developed by the Lummus Co. (32). The feedstock can be a saturated hydrocarbon or chlorohydrocarbon and the process is suited to the production of C₁ and C₂ chlorohydrocarbons.

Thermal Cracking. Thermal chlorination of ethylene yields the two isomers of tetrachloroethane, 1,1,1,2 and 1,1,2,2. Introduction of these tetrachloroethane derivatives into a tubular-type furnace at temperatures of 425–455°C gives good yields of trichloroethylene (33). In the cracking of the tetrachloroethane stream, introduction of ferric chloride into the 460°C vapor-phase reaction zone improves the yield of trichloroethylene product.

Chlorinated Aromatic Derivatives

Aromatic compounds may be chlorinated with chlorine in the presence of a catalyst such as iron, ferric chloride, or other Lewis acids. The halogenation reaction involves electrophilic displacement of the aromatic hydrogen by halogen. Introduction of a second chlorine atom into the monochloro aromatic structure leads to ortho and para substitution. The presence of a Lewis acid favors polarization of the chlorine molecule, thereby increasing its electrophilic character. Because the polarization does not lead to complete ionization, the reaction should be represented as shown in equation 26.



Continuous chlorination of benzene at 30–50°C in the presence of a Lewis acid typically yields 85% monochlorobenzene. Temperatures in the range of 150–190°C favor production of the dichlorobenzene products. The para isomer is produced in a ratio of 2–3 to 1 of the ortho isomer. Other methods of aromatic ring chlorination include use of a mixture of hydrogen chloride and air in the presence of a copper–salt catalyst, or sulfuryl chloride in the presence of aluminum chloride at ambient temperatures. Free-radical chlorination of toluene successively yields benzyl chloride, benzal chloride, and benzotrichloride. Related chlorination agents include sulfuryl chloride, *tert*-butyl hypochlorite, and *N*-chlorosuccinimide which yield benzyl chloride under the influence of light, heat, or radical initiators.

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METHYL CHLORIDE

Methyl chloride [74-87-3] (chloromethane, monochloromethane), CH₃Cl, at ordinary temperatures and pressures is a colorless gas with a very mild odor and sweet taste. Millions of kilograms of methyl chloride are produced naturally every day, primarily in the oceans. Methyl chloride is handled commercially as a liquid. It is miscible with the principal organic solvents and only slightly soluble in water. The dry liquid is stable and noncorrosive; however, in the presence of moisture, the liquid slowly decomposes and becomes corrosive to metals, particularly aluminum, zinc, and magnesium. Gaseous methyl chloride is moderately flammable. Prolonged exposure to high concentrations of the vapor can produce severe toxic effects. Methyl chloride is used mainly in the manufacture of silicones, synthetic rubber, and as a general methylating agent; its refrigerant and extractant applications now have secondary importance. Impure methyl chloride was produced in the laboratory as early as 1835 by Dumas and Peligot, who heated wood spirit, ie, crude methyl alcohol, with a mixture of sulfuric acid and common salt. It was later made by Schiff and by Walker and Johnson by the reaction of phosphorus chlorides with methyl alcohol. One of the first preparations of pure methyl chloride was probably that of Groves in 1874. Groves passed hydrogen chloride into a boiling solution of zinc chloride in twice its weight of wood spirit. Berthelot obtained the compound by chlorinating methane.

During the last quarter of the nineteenth century, methyl chloride was manufactured on a small scale in Europe for use as a refrigerant and in the synthesis of dyes. Large-scale production began in the United States about 1920, chiefly to meet refrigerant requirements. Manufacture in the United Kingdom began in 1930. Production increased greatly after 1943 when methyl chloride was required as the starting material for methyl silicones and fluorinated refrigerants. After World War II, methyl chloride production in the United States increased more than tenfold and in the late 1980s was between 3.6 and 4.5 × 10⁸ kg per year.

Physical and Chemical Properties

The physical properties of methyl chloride are listed in Table 1. Values for vapor pressure, density of liquid and saturated vapor, and enthalpy of liquid methyl chloride are given in Table 2 (1). Methyl chloride is the simplest chlorinated hydrocarbon. Dry methyl chloride in the absence of air does not decompose at an appreciable rate at temperatures approaching 400°C, even in contact with many metals. Thermal dissociation is virtually complete at 1400°C. Oxidative breakdown of the gas requires temperatures of several hundred degrees. Methyl chloride is decomposed by an open flame to give hydrogen chloride and carbon dioxide, with possible formation of small amounts of carbon monoxide and phosgene. The burning velocity of the simple chloroparaffins is inversely proportional to chlorine content (2). Methyl chloride has a burning velocity of 10.9 cm s, whereas butyl chloride burns at 31.6 cm s.

Table 1. Physical Properties of Methyl Chloride

Property	Value
mol wt	50.49
mp, °C	97.7
bp, °C at	
101.3 kPa ^a	23.73
13.3 kPa ^a	61.7
1.3 kPa ^a	92.1
sp gr	
liq, 20 °C	0.920
gas, 0°C, 101.3 kPa ^a (air = 1)	1.74
density, g L ^b	2.3045
refractive index	
liq, 23.7°C	1.3712
gas, 25°C	1.0007
surface tension, mN m (dyn cm)	
0°C	19.5
10°C	17.8
20°C	16.2
specific heat, liq, J g ^c	
20°C	1.599
15 to 30°C (av)	1.574
C _p , 25°C, 103.4 kPa ^a	0.199
C _i , 25°C	0.155
critical temperature, °C	143.1
critical pressure, kPa ^a	6679.2
critical density, g cm ³	0.353
critical volume, cm ³ g	2.833
flash point (open cup), °C	46
autoignition temperature, °C	632
flammability limits in air, vol %	10.7–17.4
combustion velocity, cm s	10.9
diffusivity in air, 25°C, 101.3 kPa, ^a cm ² s	0.105
coefficient of cubical expansion, liquid, 30 to 30°C (av)	0.00209
dielectric constant	
liq, 250°C	12.93
gas, 21°C	1.0109

dipole moment, Cm ^d	6.20 × 10 ⁻³⁰
heat of formation, ideal gas, 25°C, kJ mol ^c	81.92
free energy of formation, ideal gas, 25°C, kJ mol ^c	58.41
latent heat of fusion, J g ^c	129.7
latent heat of evaporation at bp, J g ^c	428.4
solubility of methyl chloride in water, 25°C g 100 g H ₂ O	0.48
solubility of water in methyl chloride, 25°C, g 100 g CH ₃ Cl	0.0725
solubility of methyl chloride gas, 20°C, 101.3 kPa ^a , mL 100 mL solvent	
benzene	4723
carbon tetrachloride	3756
glacial acetic acid	3679
absolute alcohol	3740

^a To convert kPa to mm Hg, multiply by 7.5.

^b At sea level, 45 ft latitude, 0°C, 101.3 kPa. ^a

^c To convert J to cal, divide by 4.184.

^d To convert Cm to debye, divide by 3.336 × 10⁻³⁰.

Table 2. Temperature Dependence of Vapor Pressure, Density, and Enthalpy of Methyl Chloride

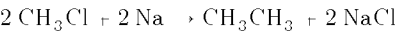
Temperature, 0°C	Vapor pressure, kPa ^a	Density		Enthalpy, kJ kg ^b		
		Liquid, g mL	Satd vapor, m ³ kg	Satd liquid	Vaporization	Satd vapor
60	15.6	1.0799	2.23	409.82	460.54	870.36
50	28.0	1.0620	1.295	424.42	425.18	876.60
40	47.4	1.0438	0.794	439.12	443.60	882.72
30	76.7	1.0253	0.508	454.12	434.54	888.66
20	118.8	1.0064	0.338	469.22	425.22	894.44
10	177.2	0.9871	0.233	484.42	415.59	900.01
0	255.7	0.9674	0.1648	500.00	405.07	905.07
10	358.2	0.9472	0.1198	516.12	393.64	909.76
20	489.3	0.9264	0.0891	531.57	382.50	914.07
30	652.5	0.9049	0.0675	547.65	370.88	917.93
40	851.6	0.8826	0.0520	563.96	357.39	921.32
50	1092	0.8595	0.0480	580.39	343.90	924.29
60	1375	0.8353	0.0324	597.01	329.75	926.76

^b To convert J to cal, divide by 4.184.

^a To convert kPa to mm Hg, multiply by 7.5.

Methyl chloride breaks down to hydrogen chloride, hydrogen, and carbon when in contact with reduced nickel in the presence of excess hydrogen at 210°C (3). It is reduced to methane by heating with calcium hydride at 180°C (4). If the liquid is heated in the presence of moisture, slow hydrolysis to methanol and hydrogen chloride occurs below 100°C. Methyl chloride is readily hydrolyzed by boiling dilute sodium hydroxide solution. At 120°C and 620 kPa (90 psi) methyl chloride saturated with water decomposes at the rate of ca 1 g 100 mL H₂O per hour. A crystalline hydrate [20604-36-8], CH₃Cl·6H₂O, is formed by subjecting water and methyl chloride to low temperatures. This system has been well studied (5). The quadruple point in the phase diagram is at 20.6°C and 506.9 kPa (5 atm).

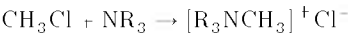
Dry methyl chloride is unreactive with all common metals except the alkali and alkaline-earth metals, magnesium, zinc, and aluminum. In dry ether solution, methyl chloride reacts with sodium to yield ethane by the Wurtz synthesis:



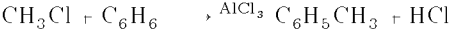
By the same reaction, methyl chloride can be condensed with higher chloroparaffins to give propane, butane, etc. Methyl chloride reacts with magnesium to form the Grignard reagent methylmagnesium chloride, CH₃MgCl, which has been applied to the synthesis of alcohols and to the preparation of intermediates for the formation of silicone polymers. The reaction with zinc is similar to that with magnesium. Dry methyl chloride vapor does not attack aluminum or its alloys at temperatures up to 60°C. In a damp atmosphere, the alloys, particularly those containing magnesium, are attacked. Reactions with aluminum catalyzed by aluminum chloride can take place with explosive violence.

Methyl chloride can be converted into methyl iodide or bromide by refluxing in acetone solution in the presence of sodium iodide or bromide. The reactivity of methyl chloride and other aliphatic chlorides in substitution reactions can often be increased by using a small amount of sodium or potassium iodide as in the formation of methyl aryl ethers. Methyl chloride and potassium phthalimide do not readily react to give *N*-methylphthalimide unless potassium iodide is added. The reaction to form methylcellulose and the Williamson synthesis to give methyl ethers are catalyzed by small quantities of sodium or potassium iodide.

Methyl chloride reacts with ammonia alcoholic solution or in the vapor phase by the Hofmann reaction to form a mixture of the hydrochlorides of methylamine, dimethylamine, trimethylamine, and tetramethylammonium chloride. With tertiary amines, methyl chloride forms quaternary derivatives.

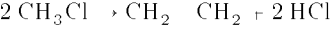


Methyl chloride, as a typical aliphatic chloride, may be used in the Friedel-Crafts reaction (qv):



Methylation of aromatic molecules can also be achieved in the vapor phase, over a solid catalyst.

When heated to very high temperatures, methyl chloride couples giving ethylene according to the reaction:



Catalytic reactions at somewhat lower temperatures also produce ethylene and other olefins. When coupled with a methane process to methyl chloride, this reaction results in a new route to the light hydrocarbons that is of considerable interest.

Manufacture

The two principal processes for the industrial production of methyl chloride are reaction of hydrogen chloride and methanol, and chlorination of methane. Several variants of both processes are used. Chlorination of methane yields other chlorinated hydrocarbons in substantial amounts; indeed, under certain conditions, methyl chloride may not be the principal product. Because the coproducts, eg, methylene chloride, chloroform, and carbon tetrachloride, are as commercially important as methyl chloride, methane chlorination can be regarded as a multiple product process rather than one with several by-products. The methanol–hydrogen chloride reaction yields methyl chloride as the main product with small amounts of dimethyl ether as the only by-product. It is commercially carried out in both liquid-phase and gas-phase processes. Hydrogen chloride is often the determining factor in choosing the best route to produce methyl chloride. The chlorination route produces HCl while the hydrochlorination route consumes HCl. The separation of unreacted methane and hydrogen chloride by-product in the chlorination process is most easily, and most often, done by absorbing the HCl in water. If there is a sufficiently large use for aqueous HCl, this process is viable to make methyl chloride on an industrial scale. Solvay describes a process whereby the methane and hydrogen chloride are separated without the use of water (6). The methanol hydrochlorination process is a user of either anhydrous HCl or aqueous hydrochloric acid. The liquid-phase process can use either form of hydrogen chloride. If anhydrous HCl is available, the gas-phase hydrochlorination process is viable. Dimethyl ether produced in both hydrochlorination processes can easily be recovered as methyl chloride by a catalytic, gas-phase process.

Thermal chlorination of methane was first put on an industrial scale by Hoechst in Germany in 1923. At that time, high pressure methanol synthesis from hydrogen and carbon monoxide provided a new source of methanol for production of methyl chloride by reaction with hydrogen chloride. Prior to 1914 attempts were made to establish an industrial process for methanol by hydrolysis of methyl chloride obtained by chlorinating methane.

Chlorination of Methane. Methane can be chlorinated thermally, photochemically, or catalytically. Thermal chlorination, the most difficult method, may be carried out in the absence of light or catalysts. It is a free-radical chain reaction limited by the presence of oxygen and other free-radical inhibitors. The first step in the reaction is the thermal dissociation of the chlorine molecules for which the activation energy is about 84 kJ mol (20 kcal mol), which is 33 kJ (8 kcal) higher than for catalytic chlorination. This dissociation occurs sufficiently rapidly in the 400 to 500°C temperature range. The chlorine atoms react with methane to form hydrogen chloride and a methyl radical. The methyl radical in turn reacts with a chlorine molecule to form methyl chloride and another chlorine atom that can continue the reaction. The methane raw material may be natural gas, coke oven gas, or gas from petroleum refining.

In a typical thermal chlorination process, the chlorine–methane mixture, with an excess of methane, is fed to a reactor where it mixes with gas previously subjected to reaction. By regulating the chlorine gas flow rate and, consequently, the heat produced by the chlorination reaction, the temperature is maintained at 400–500°C. The gas from the reactor is cooled and the hydrogen chloride removed by water washing in a packed tower. Hydrochloric acid thus obtained is generally commercially salable and is, therefore, advantageous to the economics of the process. Finally, the product gas is scrubbed with caustic liquor, dried by refrigeration, and further cooled to effect its liquefaction. Uncondensed methane is returned to the reactor. The liquefied gas is then fractionally distilled. On fractionation, a typical reaction product yields 35 wt % methyl chloride, 45 wt % methylene chloride, and 20 wt % chloroform plus a small amount of carbon tetrachloride. The relative amounts of these components can be changed by varying the reaction conditions. Solvay (6) suggests using cold, recycled liquid products to absorb the HCl. The noncondensable methane is then recycled back to the reactor. The HCl-containing products are then subjected to sequential distillations. The elimination of water greatly simplifies this process.

Variants of the methane chlorination route are the Hoechst method (7), in which a small quantity of oxygen is present; and a method (8) which uses sulfur monochloride either as catalyst or as the solvent in which the reaction takes place (9). Chlorination of methane to methyl chloride has been effected in a ternary melt of potassium-, cuprous-, and cupric chlorides at 425–500°C and in a fluidized bed of alumina gel impregnated with a potassium chloride–copper chloride melt; both methods produce approximately the same product mixture of methyl chloride and higher chlorohydrocarbons (10). The McBee-Hass technique of controlled high temperature chlorination (11) can be used to vary ratios of the chloromethanes in the product from almost 100% methyl chloride to carbon tetrachloride exclusively. High selectivities to methyl chloride can be obtained catalytically (12,13) or photochemically (14). Methyl chloride can be coproduced with other products. Mitsubishi (15) describes a high temperature process using ammonium chlorite instead of chlorine, coproducing methyl chloride and ammonia. Processes for the coproduction of trichloroethylene (16) or 1,1,2-trichloroethane (17) with methyl chloride have also been developed.

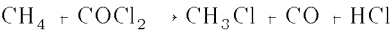
Methanol–Hydrogen Chloride Reaction.

Liquid Phase. The methyl chloride process with the widest use in the United States is the liquid-phase methanol hydrochlorination process. Silicone producers use methyl chloride in its manufacture and produce an aqueous hydrochloric acid stream as a by-product. This by-product HCl is converted back to methyl chloride by hydrochlorination. In fact, it is possible to produce methyl chloride directly from the chloromethylsilane hydrolysis step in the silicone process (18,19) (see SILICON COMPOUNDS, SILICONES).

Liquid mixtures of methanol and hydrochloric acid slowly yield methyl chloride even at 0°C (20,21). The typical process is carried out by contacting the alcohol with hydrochloric acid at 70 to 160°C and 0.1–1 MPa (15–150 psig) in the presence of a catalyst such as zinc chloride, quaternary amines (18,19,22), or with no catalyst at all (23,24). Typically 0.5 to 3% of the methanol is converted to dimethyl ether. Product methyl chloride is taken out of the reactor as a vapor and is cooled to condense as much of the water vapor and HCl as possible. Dimethyl ether and the residual water is then removed and the finished methyl chloride is condensed.

Gas Phase. The gas-phase methanol hydrochlorination process is used more in Europe and Japan than in the United States, though there is a considerable body of literature available. The process is typically carried out as follows: vaporized methanol and hydrogen chloride, mixed in equimolar proportions, are preheated to 180–200°C. Reaction occurs on passage through a converter packed with 1.68–2.38 mm (8–12 mesh) alumina gel at ca 350°C. The product gas is cooled, water-scrubbed, and liquefied. Conversions of over 95% of the methanol are commonly obtained. Gamma-alumina has been used as a catalyst at 295–340°C to obtain 97.8% yields of methyl chloride (25). Other catalysts may be used, eg, cuprous or zinc chloride on active alumina, carbon, silica, or pumice (26–30); silica–aluminas (31,32); zeolites (33); attapulgus clay (34); or carbon (35,36). Space velocities of up to 300 h⁻¹, with volumes of gas at STP per hour per volume catalyst space, are employed.

Other Reactions Producing Methyl Chloride. Many other reactions lead to the formation of methyl chloride; some have been proposed as the bases of industrial processes. The most notable of these is methane oxychlorination. A number of patents were obtained by Lummus in the mid- to late 1970s on a higher temperature, molten salt oxychlorination process (37,38). Catalyst development work has continued and generally consists of mixtures of Cu, Ni, Cr, or Fe promoted with an alkali chloride (39–42). However, there are no industrial examples of the process at this time. Good yields of methyl chloride are obtained in the reaction of dimethyl ether with hydrogen chloride in the presence of water at about 80–240°C and under sufficient pressure to maintain the water as a liquid. Dimethyl ether for this process is obtained as a by-product from methanol hydrochlorination or as a waste from methylcellulose manufacture (43). A process for the preparation of methyl chloride from carbon monoxide, hydrogen, and a halogen source such as hydrogen chloride or chlorine has been patented (44–47). Dimethyl sulfate reacts with aluminum chloride at ordinary temperature or with sodium chloride at elevated temperature to give methyl chloride (48,49). Some methyl chloride results when monochlorodimethyl ether is decomposed with zinc (50). Methane, heated with phosphene at 400°C, is chlorinated to methyl chloride (51) as follows:



Methanol, heated at 250°C with chloroform or carbon tetrachloride in contact with active carbon, is converted in part to methyl chloride (52). Methyl chloride has been produced from methoxymagnesium chloride, CH₃OMgCl, a by-product from the manufacture of certain organo–silicon compounds, by heating over 200°C (53).

Handling

All persons who have occasion to use or handle methyl chloride should be thoroughly instructed and adequately supervised in the proper methods of handling the substance to prevent or minimize exposure to the liquid or its vapors and in the proper methods of disposing of this chemical.

Methyl chloride is transported and stored as liquefied gas under pressure in cylinders, tank trucks, and tank cars. The usual cylinder capacities in the United States are 43.56 and 63.5 kg and 1 t. Cylinders may be fitted with either a short curved or long straight dip-pipe for dispensing liquid methyl chloride. Valves are normally steel and are fitted with a lead or compressed asbestos–fiber outlet washer. Teflon or Viton (for vapor service only) are recommended for gasket material. To allow for liquid expansion in the cylinders, the weight of methyl chloride contained is limited to 83° of the weight of water, which would completely fill the cylinder at 40°C, or 78° of that weight at 65°C, assuming equal coefficients of expansion. The latter limit is observed when the full cylinders will be subjected to tropical temperatures. Similar filling ratios are employed for other containers. Contact with zinc, aluminum, magnesium, and die castings should be prevented.

Methyl chloride can be supplied in horizontal cylinders of 544–590 kg capacity with valves similar to those mentioned above. Methyl chloride tank cars in the United States have a capacity of 18.1 or 35.4 metric tons and tank cars are usually fitted with four valves grouped together on a manhole cover under a removable protective dome. Two of these valves connect with dip-pipes extending to the bottom of the tank; the remaining two are connected, respectively, to a pressure gauge and to the pressure-balancing pipe for use during the transfer of methyl chloride to storage vessels.

When in use, cylinders of methyl chloride are stacked valve downwards on a suitable stand and connected to the consuming plant by an adapter. To obtain all the methyl chloride, a cylinder may be heated by steam jet or by wrapping with an electric-strip resistance heater controlled to a maximum temperature of 50°C. Compressed nitrogen or natural gas can be used to maintain the flow to the receiving vessel when transferring methyl chloride from a tank car or tank truck; compressed air must never be employed for this purpose. The pipe system carrying methyl chloride should be grounded as a precaution against ignition by static electrical discharge. Liquid trapped between closed valves after methyl chloride has been discharged could expand and burst a joint in the line. To prevent this, the valve at the discharging vessel should be closed first; after the pressure has fallen, the valve at the discharge end of the line can be closed. Fusible safety plugs fitted to tanks and other vessels containing methyl chloride under pressure are customary in the United States. Leakage of methyl chloride from plant or storage vessels must not be investigated by means of a halide lamp; in most instances a leak can be readily located by application of soap solution as the escaping gas forms observable bubbles.

Economic Aspects

Production and sales data for methyl chloride, as reported by the U.S. International Trade Commission for the years 1945 to 1989, are given in Table 3. Production grew tremendously in the 1960s and again in the late 1980s. Methanol hydrochlorination was used to produce about 64° of the methyl chloride in 1969 and about 98° by 1974. The principal U.S. producers and their capacities are shown in Table 4 (54). These capacities do not include the 100 + million kg per year used by The Dow Chemical Company, Occidental, and Vulcan to captively produce other chloromethanes.

Table 3. U.S. Methyl Chloride Production and Price Statistics

Year	Total production, 10 ³ t	Total sales, 10 ³ t	Total value, 10 ³ \$	Unit value, \$ kg
1945	13.47	12.52	4.14	0.33
1955	16.47	11.84	3.13	0.26
1965	85.05	43.00	6.64	0.15
1970	191.73	79.83	10.56	0.13
1971	198.45	87.59	11.59	0.13
1972	205.71	94.35	10.40	0.11
1973	246.80	103.10	13.64	0.13
1974	223.67	97.39	19.32	0.20
1975	166.24	65.59	20.24	0.31
1977	216.35	89.06	26.87	0.31
1978	206.28	91.27	28.98	0.31
1979	210.38	102.18	33.92	0.33
1980	164.69	75.44	29.53	0.40
1981	184.21	86.59	33.32	0.37
1982	166.53	97.63	38.16	0.40
1983	186.02	114.98	41.95	0.37
1984	219.30	121.93	51.54	0.42
1985		79.14	36.56	0.46
1986	274.85			
1987	169.66			
1988	271.40	94.86	40.36	0.42
1989	208.91	93.76	38.78	0.41

Table 4. U.S. Methyl Chloride Producers^a

Producer	Capacity, 10 ³ t yr
The Dow Chemical Company, Freeport, Tex.	22.7
The Dow Chemical Company, Plaquemine, La.	68.2
Dow Corning, Carrollton, Ky.	90.9
Dow Corning, Midland, Mich.	22.7
General Electric, Waterford, N.Y.	40.9
LCP, Moundsville, W. Va.	11.4
Occidental, Belle, W. Va.	29.5
Vista, Lake Charles, La. ^b	52.3
<i>Total</i>	<i>338.6</i>

^a Ref. 54.

^b Vulcan has recently bought out Vista.

The historical growth rate (1979–1988) for methyl chloride is 1.7° per year. The projected growth rate through 1993 is 1 to 2° per year. The projected demand in 1993 is 264,000 t. Methyl chloride is used primarily in the manufacture of silicones (Table 5).

Table 5. Uses of Methyl Chloride

Year

Use	1970	1974	1989
silicones intermediate	38 ^o o	50 ^o o	74 ^o o
tetramethyllead intermediate	38 ^o o	30 ^o o	0 ^o o
butyl rubber (catalyst solvent)	5 ^o o	5 ^o o	2 ^o o
other	19 ^o o	15 ^o o	24 ^o o
agriculture chemicals			7 ^o o
methylcellulose			6 ^o o
quaternary amines			5 ^o o
exports			4 ^o o
miscellaneous			2 ^o o

Standards.

A representative technical grade of methyl chloride contains not more than the following indicated quantities in ppm of impurities: water, 100; acid, such as HCl, 10; methyl ether, 20; methanol, 50; acetone, 50; residue, 100. No free chlorine should be detectable. Traces of higher chlorides are generally present in methyl chloride produced by chlorination of methane. The boiling point should be between −24 and −23°C, and 5–95% should distill within a range of about 0.2°C. It should be clear, colorless, and free from visible impurities.

Analysis

The most widely used method of analysis for methyl chloride is gas chromatography. A capillary column medium that does a very good job in separating most chlorinated hydrocarbons is methyl silicone or methyl (5% phenyl) silicone. The detector of choice is a flame ionization detector. Typical molar response factors for the chlorinated methanes are methyl chloride, 2.05; methylene chloride, 2.2; chloroform, 2.8; carbon tetrachloride, 3.1, where methane is defined as having a molar response factor of 2.00. Most two-carbon chlorinated hydrocarbons have a molar response factor of about 1.0 on the same basis.

There is no specific color or other reaction by which methyl chloride can be detected or identified. Quality testing of methyl chloride for appearance, water content, acidity, nonvolatile residue, residual odor, methanol, and acetone is routinely done by production laboratories. Water content is determined with Karl Fischer reagent using the apparatus by Kieselbach (55). Acidity is determined by titration with alcoholic sodium hydroxide solution. The nonvolatile residue, consisting of oil or waxy material, is determined by evaporating a sample of the methyl chloride at room temperature. The residue is examined after evaporation for the presence of odor. Methanol and acetone content are determined by gas chromatography.

Toxicity

Methyl chloride is one of the more toxic of the chlorinated hydrocarbons, and there is no adequate warning of the presence of harmful concentrations. The delay in the development of symptoms is characteristic of the toxic effect of methyl chloride. The signs and symptoms of intoxication may not develop for several hours after termination of exposure and may become progressively worse for several days before improvement begins or death occurs. Repeated exposure to low concentrations damages the central nervous system, and, less frequently, the liver, kidneys, bone marrow, and cardiovascular system (56). Methyl chloride intoxication causes headache, blurred vision, loss of coordination, and reversible personality change involving moroseness, depression, and anxiety. Routine urine and blood tests have no diagnostic value (57). Massive methyl chloride inhalation has produced myocardial damage (58). Daily exposure to concentrations of 500 ppm is extremely dangerous, even for a period of two weeks or less (59). The OSHA personal exposure level guideline and the ACGIH TLV are 50 ppm.

Uses

The principal uses of methyl chloride, as reported by the U.S. Tariff Commission, are given in Table 5. More recent analyses by the *Chemical Marketing Reporter* give the breakdown in 1989 and show significant changes in the end use pattern.

Regulation

Methyl chloride as well as the other chlorinated methanes are heavily regulated at the national, state, and local level. The manufacturing, storage, and disposal of methyl chloride may be regulated. Methyl chloride is reportable under SARA 312 (inventory) and 313 (emissions). In addition, the nonpermitted release of methyl chloride is reportable at a 100 pound (45.5 kg) quantity under CERCLA. Finally, fugitive monitoring regulations and programs may apply to individual facilities. The discharge of methyl chloride to the waterways may be regulated under OCPSF guidelines or other permitted parameters. Disposal of methyl chloride and methyl chloride-containing wastes may be regulated under RCRA as a listed discarded commercial chemical (U045) or a characteristically hazardous waste. The potential exposure to methyl chloride by workers may be regulated by OSHA or the state Industrial Hygiene Department. In addition, various state and local regulations may impose other reporting and regulatory standards. Contacting the Environmental or Regulatory Compliance Department before importing, purchasing, selling, using, or disposing of methyl chloride is strongly recommended.

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METHYLENE CHLORIDE

Methylene chloride [75-09-2] (dichloromethane, methylene dichloride), CH₂Cl₂, is a colorless, heavy liquid with a pleasant ethereal odor. Its outstanding solvent properties are the basis of its principal industrial interest. It was first prepared in 1840 by Regnault by chlorinating methyl chloride in sunlight. The compound was made in 1868 by Perkin by reducing chloroform with zinc dust and hydrochloric acid; he described this at the annual meeting of the British Association and reported its identity as "Regnault's chlorinated chloride of methyl." Butlerow made a thorough investigation of the compound in 1869. Methylene chloride became an industrial chemical of importance during World War II and, during the postwar period, its output underwent a fivefold expansion in the United States. Production reached its zenith in the late 1970s and early 1980s when the methylene chloride market began to shrink because of 1985 National Toxicology Program (NTP) study that indicated carcinogenicity in mice.

Physical and Chemical Properties

The physical properties of methylene chloride are listed in Table 1 and the binary azeotropes in Table 2. Methylene chloride is a volatile liquid. Although methylene chloride is only slightly soluble in water, it is completely miscible with other grades of chlorinated solvents, diethyl ether, and ethyl alcohol. It dissolves in most other common organic solvents. Methylene chloride is also an excellent solvent for many resins, waxes, and fats, and hence is well suited to a wide variety of industrial uses. Methylene chloride alone exhibits no flash or fire point. However, as little as 10 vol % acetone or methyl alcohol is capable of producing a flash point.

Table 1. Properties of Methylene Chloride

Property	Value
mol wt	84.92
bp at 101.3 kPa, °C	39.8
fp, °C	96.7
sp gr at 20°C	1.320
density at 20°C, kg m ³	1315.7
vapor density (air = 1.02)	2.93
diffusivity in air, m ² s	9 × 10 ⁻⁵
refractive index at 20°C	1.4244
coefficient of cubical expansion at 20–35°C	0.0014
viscosity at 20°C mPas (cP)	0.43
surface tension, mN m (dyn cm)	
at 20°C	0.02812
at 30°C	0.02654
heat of vaporization at 20°C, kJ kg ^b	329.23
thermal capacity, liq, 15–45°C (kJ kg K) ^c	1.171
heat capacity at 25°C, J mol ^c	54.09
heat of combustion, MJ kg ^c	7.1175
critical density, kg m ³	472
critical temperature, °C	245.0
critical pressure, MPa ^d	6.171
vapor pressure, kPa ^a	
at 0°C	19.6
at 20°C	46.5
at 30°C	68.1
solubility in water at 20°C, g kg	13.2
water solubility in methylene chloride at 20°C, g kg	1.4
kauri-butanol value	136
autoignition temperature, °C	640
flash point (ASTM D1310-67)	none
explosive limits at 250°C, vol % in air	14–25
electrical properties at 24°C	
dielectric strength, V cm ^e	94.488
specific resistivity at 24°C, Ωcm	1.81 × 10 ⁸
dielectric constant at 24°C, 100 kHz	10.7

^a To convert kPa to mm Hg, multiply by 7.5.

^b To convert kJ kg to Btu lb, multiply by 0.4302.

^c To convert J to cal, divide by 4.184.

^d To convert MPa to atm, divide by 0.101.

^e To convert V cm to V 100 mils, multiply by 0.254.

Table 2. Binary Azeotropes of Methylene Chloride

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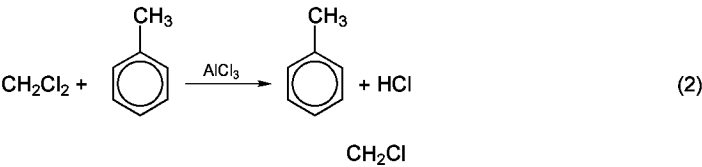
Second component			
Name	Bp, °C	Bp of azeotrope, °C	CH ₂ Cl ₂ , wt %
water	100.0	38.1	98.5
methanol	64.7	39.2	94.0
<i>t</i> -butyl alcohol	82.8	57.1	94.0
2-propanol	82.3	56.6	92.0
ethanol	78.4	54.6	88.5
iodomethane	42.5	39.8	79.0
propylene oxide	35.0	40.6	77.0
cyclopentane	49.5	38.0	70.0
diethyl ether	34.6	40.8	70.0
acetone	56.5	57.6	70.0
carbon disulfide	46.3	37.0	61.0
diethylamine	55.5	52.0	45.0

Methylene chloride is one of the more stable of the chlorinated hydrocarbon solvents. Its initial thermal degradation temperature is 120°C in dry air (1). This temperature decreases as the moisture content increases. The reaction produces mainly HCl with trace amounts of phosgene. Decomposition under these conditions can be inhibited by the addition of small quantities (0.0001–1.0%) of phenolic compounds, eg, phenol, hydroquinone, *p*-cresol, resorcinol, thymol, and 1-naphthol (2). Stabilization may also be effected by the addition of small amounts of amines (3) or a mixture of nitromethane and 1,4-dioxane. The latter diminishes attack on aluminum and inhibits iron-catalyzed reactions of methylene chloride (4). The addition of small amounts of epoxides can also inhibit aluminum reactions catalyzed by iron (5). On prolonged contact with water, methylene chloride hydrolyzes very slowly, forming HCl as the primary product. On prolonged heating with water in a sealed vessel at 140–170°C, methylene chloride yields formaldehyde and hydrochloric acid as shown by the following equation (6).



At 180°C, reaction with water results in formic acid, methyl chloride, methanol, hydrochloric acid, and some carbon monoxide.

Dry methylene chloride does not react with the common metals under normal conditions; however, a reaction with aluminum can be initiated, sometimes explosively, by the addition of small amounts of other halogenated solvents or an aromatic solvent (7). Iron catalyzes the reaction, and this can be significant in the handling and storage of methylene chloride and in the formulation of products, eg, in aluminum aerosol containers of pigmented paints, where the conditions necessary for the reaction are commonly found. A typical reaction in this process is shown in equation 2.



Further dechlorination may occur with the formation of substituted diphenylmethanes. If enough aluminum metal is present, the Friedel-Crafts reactions involved may generate considerable heat and smoke and substantial amounts of hydrogen chloride, which reacts with more aluminum metal, rapidly forming AlCl₃. The addition of an epoxide inhibits the initiation of this reaction by consuming HCl. Alkali, alkaline-earth, magnesium, and zinc metals also present a potential reactivity hazard with chlorinated solvents such as methylene chloride.

The most common reaction of methylene chloride is its reaction with chlorine to give chloroform and carbon tetrachloride. This occurs by a free-radical process initiated by heat or light in the gas or liquid phase. Catalytic chlorination to these same products is also known (see CHLOROCARBONS AND CHLOROHYDROCARBONS, CHLOROFORM).

In the gas phase, methylene chloride reacts with nitrogen dioxide at 270°C to yield a gaseous mixture consisting mainly of carbon monoxide, nitric oxide, and hydrogen chloride (8).

Methylene chloride is easily reduced to methyl chloride and methane by alkali metal ammonium compounds in liquid ammonia. When the vapor is contacted with reduced nickel at 200°C in the presence of excess hydrogen, hydrogen chloride and elementary carbon are produced. Heating with alcoholic ammonia at 100–125°C results in hexamethylenetetramine, (CH₂)₆N₄, a heterocyclic compound; with aqueous ammonia at 200°C, hydrogen chloride, formic acid, and methylamine are produced.

Bromochloromethane is produced by reaction of an excess of a mixture of methylene chloride and bromine with aluminum at 26 to 30°C (9).

When heated for eight hours at 200°C and 91.2 MPa (900 atm) in the presence of aluminum, methylene chloride reacts with carbon monoxide to yield chloroacetyl chloride, CH₂ClCOCl (10).

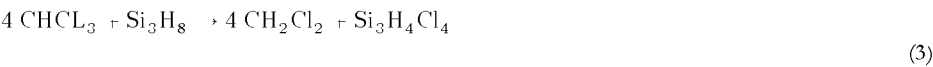
Methylene chloride vapor reacts at 300–400°C with a mixture of silicon and reduced copper under a nitrogen atmosphere to give a mixture of organosilicon derivatives (11).

Manufacture

Methylene chloride is produced industrially in the United States by two methods. The older and currently lesser used method involves a direct reaction of excess methane with chlorine at high temperatures, approximately 400–500°C, or at somewhat lower temperatures either catalytically or photolytically. This process produces methyl chloride, chloroform, and carbon tetrachloride as coproducts. The temperature and raw material flow rates to the reactor can be controlled to maximize the production of the particular chloromethane desired. The reactor effluent also contains unreacted methane and hydrogen chloride. Methane is recovered by removing the HCl by water washing and then drying before recycling. The liquid chloromethane stream, which contains the methylene chloride and its coproducts, passes through a sequence of fractionating columns after washing, alkali scrubbing, and drying (see CHLOROCARBONS AND CHLOROHYDROCARBONS, METHYL CHLORIDE (MANUFACTURE)).

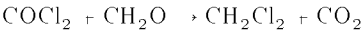
The predominant method of manufacturing methylene chloride employs as a first step the reaction of hydrogen chloride and methanol to give methyl chloride. Excess methyl chloride is then mixed with chlorine and reacts to give methylene chloride, chloroform, and carbon tetrachloride as coproducts. This reaction is usually carried out in the gas phase thermally (12) but can also be done catalytically (13,14) or photolytically (15). Parallel reactor trains operating on different feeds, CH₄–CH₃Cl or CH₃Cl–CH₂Cl₂, are known (16,17). At low temperature and high pressure, the liquid-phase process (18,19) is capable of giving high selectivities to methylene chloride.

Methylene chloride can also be made by reducing either chloroform or carbon tetrachloride with hydrogen over a platinum catalyst (20) or with metal hydrides (21). Chloroform is slowly reduced to methylene chloride upon warming with trisilane, Si₃H₈, in the absence of air as shown in equation 3.



Oxychlorination of methane can yield significant amounts of methylene chloride. A number of patents were obtained by Lummus in the mid-1970s on a high temperature, molten salt oxychlorination process (22,23). Catalyst development work has continued and generally consists of mixtures of Cu, Ni, Cr, or Fe promoted with an alkali metal (24–27). There are no industrial examples of this process at the present time.

Very high selectivities to methylene chloride can be obtained by the reaction of phosgene and formaldehyde at ca 170°C over a variety of activated carbons (28).



Ferrous hydroxide in the presence of alkaline hydroxides or carbonates reportedly reduces carbon tetrachloride to methylene chloride (29).

Economic Aspects

Table 3 lists the U.S. producers of methylene chloride and their rated yearly capacities. Since the product mix of a typical chloromethanes process is very flexible, production may be adjusted according to the demand for methylene chloride and chloroform. The demand for methylene chloride has taken a broad downturn as a result of the 1985 NTP carcinogenicity tests (Table 4). The 1988 and 1989 demands were 227,000 t and 216,000 t, respectively, with a forecast 1993 demand of 186,000 t. The historical growth rate (1979–1988) was 2.7% per year. In the future this should decrease even further to 3 to 5% per year through 1993 (31).

Table 3. U.S. Methylene Chloride Producers^a

Producer	Capacity, 10 ³ t yr
LCP, Moundsville, W.Va.	23.6
Occidental, Belle, W.Va.	40.9
The Dow Chemical Company, Freeport, Tex.	50.0
The Dow Chemical Company, Plaquemine, La.	54.5
Vulcan, Geismar, La.	36.4
Vulcan, Wichita, Kans.	59.1
<i>Total</i>	<i>264.5</i>

^a Ref. 30.

Table 4. U.S. Methylene Chloride Production and Price Statistics^a

Year	Total production, 10 ³ t	Total sales, 10 ³ t	Total value, 10 ³ \$	Unit value, \$ kg
1955	36.98	35.87	7.51	0.22
1962	71.89	64.36	11.90	0.24
1977	217.21	215.96	87.49	0.40
1978	259.14	223.04	114.32	0.51
1979	287.84	270.82	116.73	0.44
1980	256.34	145.58	70.82	0.48
1981	269.11	169.50	82.44	0.48
1982	241.94	154.95	67.04	0.44
1983	265.44	234.10	99.13	0.42
1984	275.79	227.89	117.86	0.53
1985	212.33	228.41	94.52	0.42
1986	257.46	235.99	89.04	0.37
1987	234.61	215.05	83.12	0.40
1988	229.15	234.42	91.24	0.40
1989	218.47	140.86	66.78	0.47

^a Courtesy of U.S. International Trade Commission.

Standards and Analysis

The most widely used method of analysis for methylene chloride is gas chromatography. A capillary column medium that does a very good job in separating most chlorinated hydrocarbons is methyl silicone or methyl (50% phenyl) silicone. The detector of choice is a flame ionization detector. Typical molar response factors for the chlorinated methanes are methyl chloride, 2.05; methylene chloride, 2.2; chloroform, 2.8; and carbon tetrachloride, 3.1, where methane is defined as having a molar response factor of 2.00. Most two-carbon chlorinated hydrocarbons have a molar response factor of about 1.0 on the same basis.

Although methylene chloride is considered a very stable compound, small amounts of stabilizers are usually added at the time of manufacture. Additional stabilizers may be used to provide adequate protection against corrosion or solvent breakdown in specific applications. A representative commercial grade of methylene chloride has the following specifications:

Property	Value
distillation range at 101 kPa (1 atm), IBP-DP	39.4–40.4°C
specific gravity at 25–25°C	1.319–1.322
acidity as HCl, max	5 ppm
nonvolatile matter, max	10 ppm
water, max	100 ppm
APHA color, max	10
free halogens	negative to test
residual odor	negative to test

Gas chromatographic or infrared techniques are commonly used to monitor the purity of methylene chloride shipments.

Handling

All persons who have occasion to use or handle methylene chloride should be thoroughly instructed and adequately supervised in the proper methods of handling the substance to prevent or minimize exposure to the liquid or its vapors and in the proper methods of disposing of this chemical.

Because of its low boiling point, methylene chloride should be stored in a cool place away from direct sunlight. Storage containers may be constructed of mild or plain steel that are galvanized or suitably lined. Aluminum is not recommended for bulk storage. All bulk storage tanks should be equipped with a vent dryer packed with calcium chloride or other appropriate desiccant to exclude moisture. Alternatively, the tank may utilize a dry inert gas pad with an appropriate pressure vacuum relief valve. Methylene chloride is transported in drums, truck transports, rail cars, barges, and oceangoing ships. Recommended hose-type is seamless stainless steel, Teflon, seamless bronze, or seamless steel with asbestos, Teflon, Viton, or Neoprene gaskets (32).

Toxicity

Methylene chloride is one of the least toxic chlorinated methanes. The LD₅₀ in rats is in the range of 1.6–3.0 g kg body weight. The fatal dose for a 68-kg person ranges from 80 mL (1.5–2.5 oz) to 470 mL (1 pint). Methylene chloride is painful and irritating if splashed directly into the eye. The ACGIH threshold limit value (TLV) for methylene chloride is 50 ppm by volume for an eight-hour exposure. The OSHA permissible exposure level is 500 ppm time-weighted average, 1000 ppm ceiling with 2000 ppm peak concentration. This is currently under revision.

High levels of methylene chloride vapors have an anesthetic action. The odor threshold is approximately 300 ppm. At concentrations between 310 and 800 ppm, the odor is clearly identifiable but not unpleasant. In the range of 900 to 1200 ppm, the odor is pronounced and anesthetic effects with accompanying dizziness begins after 20 minutes of exposure. Excessive exposure to levels greater than 2300 ppm causes lightheadedness, dizziness, nausea, headaches, and tingling or numbness of extremities. Mental alertness and physical coordination may also be impaired. Exposure to very high concentrations could result in unconsciousness or death.

Methylene chloride, applied to both intact and abraded skin of rabbits in doses as large as 0.5 g kg body weight per day, five times per week, for a period of 90 days, caused no apparent adverse effects. Absorption through the skin is not usually a hazard when good working practices are followed.

A determination that carbon monoxide might be a metabolite of methylene chloride in humans (33) suggests that unacceptable levels of carboxyhemoglobin would exist in the blood of persons exposed to methylene chloride vapors at concentrations greater than 500 ppm for extended periods of time. These conditions are rarely encountered in most industrial applications. However, as with any organic solvent, adequate ventilation should be provided to ensure compliance with all industrial and governmental regulations.

Studies in which pregnant rats and mice were exposed to 1250 ppm of methylene chloride for seven hours a day on days 6–15 of gestation indicated no significant maternal, embryonal, or fetal toxicity (34). Methylene chloride was shown to be nonteratogenetic to either animal at the concentration studied.

The National Toxicology Program (NTP) reported on tests on mice and rats that there was an increase in the spontaneous incidence of benign tumors in male and female rats and an increase in malignant liver and lung tumors in B6C3F1 mice. NTP concluded that these data demonstrated clear evidence of carcinogenicity in mice and female rats and some evidence in male rats (35).

Like many organic solvents, including hexane, heptane, benzene, xylene, toluene, gasoline, and particularly some of the other chlorinated and fluorinated solvents, methylene chloride may cause cardiac arrhythmias in the presence of elevated epinephrine when inhaled at concentrations as high as 20,000 ppm (36).

Fatalities have occurred when unprotected workers have entered an unventilated tank or piece of equipment that contained high vapor concentrations of a chlorinated solvent such as methylene chloride.

Uses

For use in paint strippers, one of its first applications, methylene chloride is blended with other chemical components to maximize its effectiveness against specific coatings. Typical additives include alcohols, acids, amines or ammonium hydroxide, detergents, and paraffin wax. Paint stripping formulations without methylene chloride have not as yet been shown to be as effective as those with methylene chloride.

Methylene chloride is used as an extraction solvent for the decaffeination of coffee, spices, and beer hops because of its strong solvency power and stability (37–39) and is well suited for use in the manufacture of photographic film as well as a carrier solvent in the textile industry. It is also used as a solvent for vapor degreasing of metal parts. Methylene chloride may also be blended with petroleum and other chlorinated hydrocarbons for use as a dip-type cleaner in the metal-working industry. Use in this area is falling because of recycling and recovery efforts on the part of end users. Aerosol applications are expected to continue to decline because of a government cancer-labeling requirement on consumer goods containing methylene chloride. The reduction in the use of 1,1,1-trichloroethane because of the Montreal Protocol and clean air legislation may increase the use of methylene chloride. Other applications include low pressure refrigerants, air-conditioning installations, and as a low temperature heat-transfer medium.

There are several uses for methylene chloride in chemical processing, including the manufacture of polycarbonate plastic from bisphenol and phosgene, the manufacture of photoresist coatings, and as a solvent carrier for the manufacture of insecticide and herbicide chemicals (Table 5). Methylene chloride is also used by the pharmaceutical industry as a process solvent in the manufacture of steroids, antibiotics, vitamins, and to a lesser extent as a solvent in the coating of tablets (40). Other uses include grain fumigation (41) and oil dewaxing (42).

Table 5. Uses of Methylene Chloride (1989)

paint stripper	28° o
aerosols	18° o
exports	15° o
chemical processing	11° o
urethane foam blowing agent	9° o
metal degreasing	8° o
electronics	7° o
other	4° o

Regulation

Methylene chloride, as are the other chlorinated methanes, is heavily regulated at the national, state, and local level. The manufacturing, storage, and disposal of methylene chloride may be regulated. Methylene chloride is reportable under SARA 312 (inventory) and 313 (emissions). In addition, the nonpermitted release of methylene chloride is reportable at a 1000 pound (455 kg) quantity under CERCLA. Finally, fugitive monitoring regulations and programs may apply to individual facilities. The discharge of methylene chloride to the waterways may be regulated under OCPSF guidelines or other permitted parameters. Disposal of methylene chloride and methylene chloride-containing wastes may be regulated under RCRA as a discarded commercial chemical (U080) or as a nonspecific source waste (F001 and F002). The potential exposure to methylene chloride by workers may be regulated by OSHA or the state Industrial Hygiene Department. In addition, various state and local regulations may impose other reporting and regulatory standards. Contacting the Environmental or Regulatory Compliance Department before importing, purchasing, selling, using, or disposing of methylene chloride is strongly recommended.

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CHLOROFORM

Chloroform [67-66-3] (trichloromethane, methenyl chloride), CHCl₃, at normal temperature and pressure is a heavy, clear, volatile liquid with a pleasant, ethereal, nonirritant odor. Although chloroform is nonflammable, its hot vapor in admixture with vaporized alcohol burns with a green tinged flame. Chloroform is miscible with the principal organic solvents and is slightly soluble in water. It is less stable in storage than either methyl or methylene chloride. Chloroform decomposes at ordinary temperatures in sunlight in the absence of air and in the dark in the presence of air. Phosgene is one of the oxidative decomposition products.

Chloroform was discovered in 1831 by Liebig and Soubeirain simultaneously. Liebig obtained chloroform by the action of alkali on chloral, and Soubeirain by reaction of bleaching powder with alcohol or acetone. Guthrie, in the United States, is also alleged to have discovered chloroform in 1831. In 1839, Dumas produced chloroform by heating alkali with trichloroacetic acid. In the following year, Regnault obtained it by chlorinating methyl chloride. Chloroform was first used in medicine as a stimulant, taken internally, and as an inhalant in cases of asthma. In November, 1847, on the suggestion of Waldie, a Liverpool chemist, Simpson used chloroform as a total anesthetic in obstetrics.

Shortly after Simpson's successful use of chloroform in Edinburgh, Fraser began making pure anesthetic chloroform on a small scale in Nova Scotia.

In 1900, the Pennsylvania Salt Manufacturing Co. initiated large-scale production in the United States. The Midland Chemical Co., a subsidiary of The Dow Chemical Company, began to manufacture chloroform by reducing carbon tetrachloride in 1903. Chloroform was one of the first organic chemicals produced on a large scale in the United States.

Chloroform was used chiefly as an anesthetic and in pharmaceutical preparations immediately prior to Wodd War II. However, these uses have been banned. Annual output in both the United States and the United Kingdom was between 900 and 1350 metric tons. During the war, chloroform production in the United States tripled, largely to meet the requirement for penicillin manufacture. Demand for chloroform continued to increase in the postwar period as its technical applications were extended. Consumption continues to increase at a comparatively rapid rate. Chloroform is now used primarily in the manufacture of HCFC-22, monochlorodifluoromethane, a refrigerant, and as a raw material for polytetrafluoroethylene plastics.

Physical and Chemical Properties

The physical properties of chloroform are listed in Table 1.

Table 1. Physical Properties of Chloroform

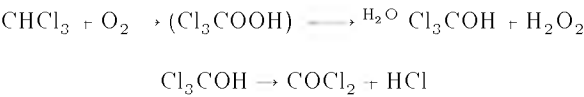
Property	Value
mol wt	119.38
refractive index at 20°C	1.4467
autoignition temperature, °C	above 1000
flash point, °C	none
mp, °C	63.2
101 MPa ^a	43.4
507 MPa ^a	20.4
1216 MPa ^a	112.6
bp at 101 kPa ^b , °C	61.3
sp gr	
0 4°C	1.52637
25 4°C	1.48069
60.9 4°C	1.4081
vapor density at 101 kPa ^b , 0°C, kg m ³	4.36
surface tension, mN m (dyn cm)	
air, 20°C	27.14
air, 60°C	21.73
water, 20°C	45.0
heat capacity at 20°C, kJ (kg·K) ^c	0.979
critical temperature, °C	263.4
critical pressure, MPa ^a	5.45
critical density, kg m ³	500
critical volume, m ³ kg	0.002
thermal conductivity at 20°C, W (m·K)	0.130
coefficient of cubical expansion	0.001399
dielectric constant, 20°C	4.9
dipole moment, Cm ^d	3.84 × 10 ⁻³⁰
heat of combustion, MJ (kgmol) ^c	373
heat of formation at 25°C, MJ (kgmol) ^c	
gas	89.66
liquid	120.9
latent heat of evaporation at bp, kJ kg ^c	247
solubility of chloroform in water, g kg H ₂ O	
0°C	10.62
20°C	8.22
30°C	7.76

solubility of water in chloroform, at 22°C, g / kg chloroform		0.806		
viscosity, liq, mPa·s (cP)				
13°C		0.855		
0°C		0.700		
20°C		0.563		
30°C		0.510		
vapor pressure	°C	kPa ^b	°C	kPa ^b
	60	0.11	0°C	8.13
	50	0.27	10°C	13.40
	40	0.63	20°C	21.28
	30	1.33	30°C	32.80
	20	2.61	40°C	48.85
	10	4.63	50°C	70.13

^a To convert MPa to atm, multiply by 9.87.
^b To convert kPa to mm Hg, multiply by 7.5.
^c To convert J to cal, divide by 4.184.
^d To convert Cm to debye, divide by 3.336 × 10^{−30}.

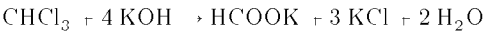
Chloroform dissolves alkaloids, cellulose acetate and benzoate, ethylcellulose, essential oils, fats, gutta-percha, halogens, methyl methacrylate, mineral oils, many resins, rubber, tars, vegetable oils, and a wide range of common organic compounds. A temperature increase occurs when chloroform is mixed with diethyl ether. Chloroform forms a series of binary azeotropes (1); the azeotrope with water boils at 56.1°C and contains 97.2% chloroform. The ternary azeotrope with ethanol and water boils at 55.5°C and contains 4 mol % alcohol and 3.5 mol % water. At 25°C, chloroform dissolves 3.59 times its volume of carbon dioxide.

Chloroform slowly decomposes on prolonged exposure to sunlight in the presence or absence of air and in the dark in the presence of air. The products of oxidative breakdown include phosgene, hydrogen chloride, chlorine, carbon dioxide, and water. At 290°C, chloroform vapor is not attacked by oxygen. In contact with iron and water hydrogen peroxide is also produced, probably by the following reaction sequence (2):



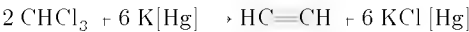
Oxidation with powerful oxidizing agents, eg, chromic acid, results in the formation of phosgene and the liberation of chlorine. Nitrogen dioxide at about 270°C oxidizes chloroform to a mixture of compounds including phosgene, hydrogen chloride, water, and carbon dioxide (3). Ozone forms a blue solution in chloroform and causes rapid decomposition.

Chloroform and water at 0°C form six-sided crystals of a hydrate, CHCl₃·18H₂O [67922-19-41], which decompose at 1.6°C. Chloroform does not decompose appreciably when in prolonged contact with water at ordinary temperature and in the absence of air. However, on prolonged heating with water at 225°C, decomposition to formic acid, carbon monoxide, and hydrogen chloride occurs. A similar hydrolysis takes place when chloroform is decomposed at elevated temperature by potassium hydroxide.



Reaction of chloroform with hydroxide, particularly in the presence of methanol, can result in an explosion.

Chloroform resists thermal decomposition at temperatures up to about 290°C. Pyrolysis of chloroform vapor occurs at temperatures above 450°C, producing tetrachloroethylene, hydrogen chloride, and a number of chlorohydrocarbons in minor amounts (4,5). Pyrolysis in contact with hot pumice is catalyzed by vaporized iodine (1%), resulting in tetrachloroethylene, hexachloroethane, and carbon tetrachloride. Hexachlorobenzene, carbon monoxide, hydrogen chloride, and titanium tetrachloride are formed when chloroform vapor is decomposed by hot titanium oxide. In contact with potassium amalgam or red-hot copper, chloroform reacts to give acetylene.



Small quantities of ethyl alcohol stabilize chloroform during storage. Various other stabilizers have been proposed, eg, CH₂=CHCH₂CH₂CN and methacrylonitrile (6).

Chloroform can be reduced to methane with zinc dust and aqueous alcohol. In the presence of a catalyst or ammonia, the reduction yields methylene chloride as well as methane.

Chloroform reacts readily with halogens or halogenating agents. Chlorination of the irradiated vapor is believed to occur by a free-radical chain reaction (7).

At 225–275°C, bromination of the vapor yields bromochloromethanes: CCl₃Br, CCl₂Br₂, and CClBr₃. Chloroform reacts with aluminum bromide to form bromoform, CHBr₃. Chloroform cannot be directly fluorinated with elementary fluorine; fluoroform, CHF₃, is produced from chloroform by reaction with hydrogen fluoride in the presence of a metallic fluoride catalyst (8). It is also a coproduct of monochlorodifluoromethane from the HF–CHCl₃ reaction over antimony chlorofluoride. Iodine gives a characteristic purple solution in chloroform but does not react even at the boiling point. Iodoform, CHI₃, may be produced from chloroform by reaction with ethyl iodide in the presence of aluminum chloride; however, this is not the route normally used for its preparation.

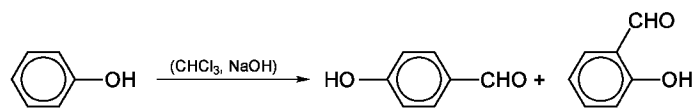
No decomposition occurs when boiling chloroform is in prolonged contact with anhydrous aluminum chloride; a double compound is formed from which unchanged chloroform is liberated by the action of water. With benzene in the presence of aluminum chloride, chloroform reacts to give triphenylmethane, (C₆H₅)₃CH, which is also formed from chloroform and phenylmagnesium bromide, C₆H₅MgBr.

In the presence of an alkali metal hydroxide at about 50°C, chloroform condenses with acetone to give 1,1,1-trichloro-2-methyl-2-propanol, [57-15-8] ie, chlorobutanol, chloretone, or acetone–chloroform (9,10). Chlorobutanol is a white crystalline substance with a camphorlike odor; its sedative, anesthetic, and antiseptic properties have given the compound some importance in the pharmaceutical industry.

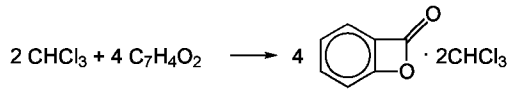
Chloroform reacts with aniline and other aromatic and aliphatic primary amines in alcoholic alkaline solution to form isonitriles, ie, isocyanides, carbylamines, as shown:



Phenylisonitrile has a powerful characteristic odor; it is used as a qualitative test (the carbylamine test) for chloroform or primary aromatic amines. Chloroform reacts with phenols in alkaline solution to give hydroxyaromatic aldehydes in the Reimer-Tiemann reaction; eg, phenol gives chiefly *p*-hydroxybenzaldehyde and some salicylaldehyde (11) (see HYDROXYBENZALDEHYDES).



Chloroform combines with the inner anhydride of salicyclic acid to form a well-defined crystalline double compound (12):



This complex readily liberates chloroform when heated and this reaction has been used to produce very pure chloroform.

Reactivities of several chlorinated solvents, including chloroform, with aluminum, iron, and zinc in both dry and wet systems have been determined, as have chemical reactivities in oxidation reactions and in reactions with amines (11). Unstabilized wet chloroform reacts completely with aluminum and attacks zinc at a rate of >250 μm yr and iron at <250 μm yr. The dry, uninhibited solvent attacks aluminum and zinc at a rate of 250 μm yr and iron at 25 μm yr.

Manufacture

Chloroform can be manufactured from a number of starting materials. Methane, methyl chloride, or methylene chloride can be further chlorinated to chloroform, or carbon tetrachloride can be reduced, ie, hydrodechlorinated, to chloroform. Methane can be oxychlorinated with HCl and oxygen to form a mixture of chlorinated methanes. Many compounds containing either the acetyl (CH₃CO) or CH₃CH(OH) group yield chloroform on reaction with chlorine and alkali or hypochlorite. Methyl chloride chlorination is now the most common commercial method of producing chloroform. Many years ago chloroform was almost exclusively produced from acetone or ethyl alcohol by reaction with chlorine and alkali.

Methane or Chloromethane Chlorination. This chlorination reaction is generally carried out in the gas phase at 400–500°C making all of the more heavily chlorinated products in substantial yields (see CHLOROCARBONS AND CHLOROHYDROCARBONS, METHYLENE CHLORIDE (MANUFACTURE)). It is carried out by mixing the organic feed with gaseous chlorine and heating to initiate the reaction. Once started, this free-radical process rapidly goes to completion with the generation of substantial amounts of heat. This heat is transferred back to heat the feed stream. The reaction is controlled by limiting the amount of one of the feeds, generally the chlorine. The use of two reactors in parallel using different organic feed compositions is known (12,13).

The product selectivity of the chlorination of methane has been adequately described (14) over the whole range of products from methyl chloride to carbon tetrachloride. The presence of partially chlorinated chloromethanes in the reactor feed stream tends to change the product mix toward the more heavily chlorinated products. These partially chlorinated chloromethanes can be gases recycled from the product recovery equipment. Thus there is a fair degree of flexibility in tailoring product selectivity. The most common feed material for this process is methyl chloride. Use of methane as a feed material generally requires the production of the less desirable aqueous HCl and is not widely used industrially. In either case, to maximize chloroform production, product methyl chloride and methylene chloride are usually recycled back to the reactor. Numerous variations have been suggested as ways to increase the selectivity to a desired product. Tokuyama Soda has developed and practices a liquid-phase process based on methyl chloride chlorination (15–17). Light-initiated processes also claim enhanced selectivity (18). A novel process where chlorine atoms, the chain carriers in the free-radical reaction, are generated and transported to a reaction zone has been described (19,20). Fluidized beds have been suggested as a method of handling the large amount of heat generated and affecting selectivity with the proper choice of catalyst (21).

Oxychlorination of Methane. The oxychlorination of methane with HCl and oxygen has received some attention since the 1970s (22–24), though there are no examples of an industrial process. This can be a coproduct process making all the chloromethanes in significant yields or one that makes primarily methyl chloride. Interest in this route has increased in the past few years because of progress in the methane to light hydrocarbons process.

Hydrogenation of Carbon Tetrachloride. Carbon tetrachloride can be hydrogenated, ie, hydrodechlorinated, to chloroform over a catalyst (25,26) or thermally (27). Although there are no industrial examples of this process at this time, it will receive more attention as more carbon tetrachloride becomes available as the CFC-11 and -12 markets decline (see, CHLOROCARBONS AND CHLOROHYDROCARBONS, CARBON TETRACHLORIDE). Chloroform can be further hydrodechlorinated to methylene chloride (28,29).

Reduction of Alcohols or Ketones. The reaction of alcohols and ketones with chlorine and base to give chloroform is well known (30). This was an industrial process for chloroform, but there are no plants currently using this technology. This reaction is possibly an important source of chloroform in the water treating process.

Economic Aspects

Chloroform production figures, sales figures, and prices in the United States for the period 1960–1989 inclusive are presented in Table 2. Annual production of chloroform remained between 900 and 1350 metric tons during the 1930s when it was used primarily for anesthetic purposes and by the pharmaceutical and fine chemical industries. During and immediately after World War II, chloroform found a new application as an extractant in the production of penicillin. Chloroform production continued to expand for use in the manufacture of chlorofluoromethane refrigerants for domestic air-conditioners (31) and as a starting material in the manufacture of polytetrafluoroethylene (PTFE). The growth rate over the period 1979 to 1988 was 3.8° per year. The projected growth rate through 1993 is 5 to 6° per year (32).

Table 2. U.S. Chloroform Production and Price Statistics^a

Year	Total production, 10 ³ t	Total sales, 10 ³ t	Total value, 10 \$	Unit value, \$ kg
1960	34.67	25.40		
1965	69.18	55.94		
1970	108.81	79.33		
1973	114.66	110.60		
1974	136.89	114.44		
1975	118.71	87.14		
1976	132.39	120.39		
1977	137.06	129.60	49.39	0.37
1978	158.71	137.32	53.42	0.40
1979	161.84	153.57	62.57	0.42
1980	160.50	154.91	71.16	0.46
1981	184.20	176.25	86.73	0.48
1982	135.87	133.83	66.57	0.51
1983	164.70	154.37	73.33	0.48
1984	183.90	151.93	86.18	0.57
1985	125.12	174.47	54.51	0.31
1986	192.01	189.28	82.12	0.44
1987	209.92	202.90	53.54	0.26

1988	238.02	246.15	99.14	0.40
1989	266.53	229.31	102.22	0.45

^a Courtesy of U.S. International Trade Commission.

This high projected growth rate is driven by the expected strong growth of the HCFC-22 and fluoropolymer markets, which account for 90% of the total chloroform market. HCFC-22 is a substitute for some applications currently using CFC-11 and CFC-12. It is restricted by the Montreal Protocol but will not be phased out until much later. This demand pushed chloroform production up 10% in both 1988 and 1989 (32).

The U.S. chloroform producers and their capacities are listed in Table 3. With this strong increasing demand and the decline in the methylene chloride market, chloroform producers have had to swing their production away from methylene chloride and toward chloroform. This capability may result in the capacities listed being somewhat understated for chloroform and overstated for methylene chloride, the primary coproduct in chloroform production.

Table 3. U.S. Chloroform Producers ^a

Producer	Capacity, 10 ³ t yr
The Dow Chemical Company, Freeport, Tex.	61.4
The Dow Chemical Company, Plaquemine, La.	68.2
LCP, Moundsville, W.Va.	18.2
Occidental, Belle, W.Va.	22.7
Vulcan, Geismar, La.	27.2
Vulcan, Wichita, Kans.	50.0
Total	247.7

^a Ref. 32.

Specifications and Standards

Technical-grade chloroform generally contains one or more stabilizers, which vary according to specification requirements. The most common is 50 ppm 2-methyl-2-butene [513-35-9]. Other stabilizers are industrial methylated spirit (0.2%), absolute alcohol (0.6–1%), thymol, *p*-butylphenol, or *n*-octylphenol (0.0005–0.01%). A representative technical quality chloroform contains the following amounts of the indicated substances (maximum):

water	50 ppm
acid (as HCl)	10 ppm
methylene chloride	200 ppm
bromochloromethane	300 ppm
carbon tetrachloride	250 ppm
1,2-dichloroethylene	100 ppm
vinylidene chloride	100 ppm
residue (on evaporation at 110°C)	10 ppm
dissolved chlorine	not detectable

Analysis

The most widely used method of analysis for chloroform is gas chromatography. A capillary column medium that does a very good job in separating most chlorinated hydrocarbons is methyl silicone or methyl (5% phenyl) silicone. The detector of choice is a flame ionization detector. Typical molar response factors for the chlorinated methanes are methyl chloride, 2.05; methylene chloride, 2.2; chloroform, 2.8; and carbon tetrachloride, 3.1, where methane is defined as having a molar response factor of 2.00. Most two-carbon chlorinated hydrocarbons have a molar response factor of about 1.0 on the same basis.

In the known absence of bromoform, iodoform, chloral, and other halogenated methanes, the formation of phenylisocnitrile with aniline provides a simple and fairly sensitive but nonspecific test for the presence of chloroform, the carbylamine test. Phenylisocnitrile formation is the identification test given in the *British Pharmacopoeia*. A small quantity of resorcinol and caustic soda solution (10% concentration) added to chloroform results in the appearance of a yellowish red color, fluorescing yellow-green. When 0.5 mL of a 5% thymol solution is boiled with a drop of chloroform and a small quantity of potassium hydroxide solution, a yellow color with a reddish sheen develops; the addition of sulfuric acid causes a change to brilliant violet, which, diluted with water, finally changes to blue (33).

Chloroform may be estimated quantitatively by determining the amount of copper oxide produced when it is warmed with Fehling's solution, which is potassium cupritartrate (34). An alternative procedure consists of heating the chloroform with concentrated alcoholic potassium hydroxide in a sealed tube at 100°C and determining the amount of potassium chloride produced (35).

Handling

All persons who have occasion to use or handle chloroform should be thoroughly instructed and adequately supervised in the proper methods of handling the substance to prevent or minimize exposure to the liquid or its vapors and in the proper methods of disposing of this chemical.

Chloroform should be stored in sealed containers in a cool place. Glass containers should be dark green or amber. Bulk storage containers may be constructed of mild or plain steel that is galvanized or suitably lined. Aluminum is not recommended for bulk storage. All bulk storage tanks should be equipped with a vent dryer packed with calcium chloride or other appropriate desiccant to exclude moisture. Alternatively, the tank may utilize a dry inert gas pad with an appropriate pressure vacuum relief valve, which is the recommended procedure, with appropriate disposal of the tank vents. Seamless stainless steel, Teflon, seamless bronze, or seamless steel hose is recommended with asbestos, Teflon, Viton, or Neoprene gaskets (36). Chloroform is transported in drums, truck transports, rail cars, barges, and oceangoing ships.

Health and Safety

The principal hazard in exposure to chloroform is damage to the liver and kidneys resulting from inhalation or ingestion. Inhalation of high concentrations may result in disturbances of equilibrium or loss of consciousness. Chloroform is mildly irritating to skin and mucous membranes upon contact, and to the alimentary tract upon ingestion. It is believed that medically significant quantities are not absorbed through intact skin.

The toxic effects of chloroform resemble those of carbon tetrachloride. The probable effects of exposure to various atmospheric concentrations of chloroform are summarized in Table 4 (37).

Table 4. Effects of Exposure to Chloroform

Concentration		Response
ppm	mg L	
390	205–310	smallest amount that can be detected by smell
	1–1.5	endured for 30 min without complaint
	1.9	definite after effects; fatigue and headache still experienced hours after exposure
	5	dizziness, intracranial pressure, and nausea after 7 min exposure
	5	dizziness and salivation after a few minutes exposure
	7.2	vomiting, sensation of fainting
	20	narcotic limiting concentration
14,340–16,400		70–80

In the past, chloroform was used extensively as a surgical anesthetic, but this use was abandoned because exposure to narcotic concentrations often resulted in sudden death from effects on the heart and circulation or from severe injury to the liver. In addition, chloroform for this and other consumer uses was banned by FDA in 1976 with the discovery that it is carcinogenic in mice (38). When splashed into the eye, chloroform causes local pain and irritation, but serious injury is not expected. Skin contact for single, brief exposures ordinarily causes little or no local irritation.

Repeated or prolonged contact with the skin, especially under clothing, may result in local irritation and inflammation, and at elevated temperatures such as in the presence of an open flame, chloroform decomposes to form by-products, including phosgene, chlorine, and hydrogen chloride, all of which are severe irritants to the respiratory tract.

Ingestion of chloroform is followed immediately by a severe burning in the mouth and throat, pain in the chest and abdomen, and vomiting. Loss of consciousness and liver injury may follow depending on the amount swallowed. The tendency of chloroform to produce liver injury is significantly augmented in alcoholics and persons with nutritional deficiencies.

The most serious hazard of repeated exposure to chloroform inhalation is injury to the liver and kidneys. Evidence indicates that in humans, repeated exposure to atmospheric concentrations well below the odor threshold may cause such injury. Industrial experience has shown that daily exposure to concentrations below 100 ppm may result in a variety of nervous system and alimentary tract symptoms, in the absence of demonstrable evidence of injury (39). Injury to the liver is similar to but somewhat less severe than that caused by carbon tetrachloride. Kidney injury is usually associated with but less severe than liver injury.

The ACGIH recommended maximum time-weighted average concentration in the workplace atmosphere for eight-hour daily exposure is 10 ppm. OSHA has set the permissible exposure level at 2 ppm. It may be desirable to exclude alcoholics, persons with chronic disorders of the liver, kidneys, and central nervous system, and those with nutritional deficiencies from working with chloroform.

Treatment of chloroform poisoning is symptomatic; no specific antidote is known. Adrenalin should not be given to a person suffering from chloroform poisoning.

Uses

About 90% of the chloroform produced goes into the production of HCFC-22 (chlorodifluoromethane [75-45-6]). Of this 90% about 70% is used as a refrigerant and about 30% is used as a starting material in the production of fluoropolymers, such as polytetrafluoroethylene (PTFE). Of the remaining 10% of the chloroform production about 8% is exported and 2% is used in other ways.

Miscellaneous uses include extraction and purification of penicillin, alkaloids, vitamins, and flavors, and as an intermediate in the preparation of dyes and pesticides. Chloroform has also been used as a fumigant and insecticide, in the formulation of cough syrups, toothpastes, liniments, and toothache preparations. These latter uses were banned by the FDA in 1976 (38).

Regulation

Chloroform and the other chlorinated methanes are heavily regulated at the national, state, and local level. The manufacturing, storage, and disposal of chloroform may be regulated. Chloroform is reportable under SARA 312 (inventory) and 313 (emissions). In addition, the nonpermitted release of chloroform is reportable at a 10 pound (4.5 kg) quantity under CERCLA. Finally, fugitive monitoring regulations and programs may apply to individual facilities. The discharge of chloroform to the waterways may be regulated under OCPSF guidelines or other permitted parameters. Disposal of chloroform and chloroform-containing wastes may be regulated under RCRA as a discarded commercial chemical (U044) or as an extractable at 6.0 mg L under the TCLP (D022). The potential exposure to chloroform by workers may be regulated by OSHA or the state Industrial Hygiene Department. In addition, various state and local regulations may impose other reporting and regulatory standards. Contacting the Environmental or Regulatory Compliance Department before importing, purchasing, selling, using, or disposing of chloroform is strongly recommended.

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CARBON TETRACHLORIDE

Carbon tetrachloride [56-23-5] (tetrachloromethane), CCl₄, at ordinary temperature and pressure is a heavy, colorless liquid with a characteristic nonirritant odor; it is nonflammable. Carbon tetrachloride contains 92 wt % chlorine. When in contact with a flame or very hot surface, the vapor decomposes to give toxic products, such as phosgene. It is the most toxic of the chloromethanes and the most unstable upon thermal oxidation. The commercial product frequently contains added stabilizers. Carbon tetrachloride is miscible with many common organic liquids and is a powerful solvent for asphalt, benzyl resin (polymerized benzyl chloride), bitumens, chlorinated rubber, ethylcellulose, fats, gums, rosin, and waxes.

Carbon tetrachloride was one of the first organic chemicals produced on a large scale. In the 1890s, commercial manufacturing processes were being investigated by the United Alkali Co. in England. At the same time it was also produced in Germany, exported to the United States, and retailed as a spotting agent under the trade name Carbona. Large-scale production of carbon tetrachloride in the United States began about 1907. By 1914, annual production fell just short of 4500 metric tons and was used primarily for dry cleaning and for charging fire extinguishers. During World War I, U.S. production of carbon tetrachloride expanded greatly; its use was extended to grain fumigation and the rubber industry. In 1934 it was supplanted as the predominant dry-cleaning agent in the United States by perchloroethylene, which is much less toxic and more stable. During the years immediately preceding World War II, trichloroethylene began to displace carbon tetrachloride from its then extensive market in the United States as a metal degreasing solvent. Carbon tetrachloride is more difficult to recover from degreasing operations, more readily hydrolyzed, and more toxic than trichloroethylene. The demands of World War II stimulated production and marked the beginning of its use as the starting material for chlorofluoromethanes, by far the most important application for carbon tetrachloride.

By the late 1940s, carbon tetrachloride was rapidly losing in competition not only with trichloroethylene but with perchloroethylene as well. In 1948 only 33% of the solvent used by the dry-cleaning industry was carbon tetrachloride and 60% was perchloroethylene; two years later the ratio of perchloroethylene to carbon tetrachloride was three to one. This technological change was not reflected in past sales of carbon tetrachloride, which exhibited a steady increase following World War II. It was at this time, ca 1950, that carbon tetrachloride found a new and rapidly expanding use as the starting material in the manufacture of fluorinated refrigerants, an application that by 1954 accounted for about half the total demand for carbon tetrachloride and over 95% of the demand today.

Physical and Chemical Properties

The physical properties of carbon tetrachloride are listed in Tables 1 and 2.

Table 1. Physical Properties of Carbon Tetrachloride

Property	Value
mol wt	153.82
mp, °C	
101.3 kPa ^a	22.92
21.3 MPa ^b	19.5
62.8 MPa ^b	0
117.5 MPa ^b	19.5
bp at 101.3 kPa ^a , °C	76.72
refractive index at 15°C	1.46305
sp gr	
0–4°C	1.63195
20–4°C	1.59472
76–4°C	1.48020
autoignition temperature, °C	>1000
flash point, °C	none
density of solid, g cm ³	
186°C	1.831
80°C	1.809
vapor density (air = 1)	5.32
surface tension, mN m (–dyn cm)	
0°C	29.38
20°C	26.77
60°C	18.16
specific heat, J kg ^c	
20°C	866
30°C	837
critical temperature, °C	283.2
critical pressure, MPa ^b	4.6
critical density, kg m ³	558
thermal conductivity, mW (mK)	
liquid, 20°C	118
vapor, bp	7.29
average coefficient of volume expansion	
0–40°C	0.00124
dielectric constant, ε	
liquid, 20°C	2.205
liquid, 50°C	1.874

vapor, 87.6°C	1.00302
heat of formation, kJ/mol ^c	
liquid	−142
vapor	−108
heat of combustion, liquid, at constant volume at 18.7°C, kJ/mol ^c	365
latent heat of fusion, kJ/mol ^c	2.535
latent heat of vaporization, kJ/kg ^c	194.7
solubility of CCl ₄ in water at 25°C, g/100 g H ₂ O	0.08
solubility of water in CCl ₄ at 25°C, g/100 g CCl ₄	0.013

^a To convert kPa to mm Hg, multiply by 7.5.
^b To convert MPa to atm, divide by 0.101
^c To convert J to cal, divide by 4.184.

Table 2. Viscosity and Vapor Pressure of CCl₄ as a Function of Temperature

Temperature, °C	Viscosity, mPas(=cP)	Vapor pressure, kPa ^a
−50		0.123
−20		1.323
0	1.329	4.41
20	0.965	11.94
40	0.739	28.12
60	0.585	58.53
100	0.383	
150		607.3
180	0.201	
200		1458

^a To convert kPa to mm Hg, multiply by 7.5.

Carbon tetrachloride readily dissolves stannic chloride, SnCl₄, but not ferric chloride, FeCl₃. Carbon tetrachloride forms a large number of binary and several ternary azeotropic mixtures; a partial list of the former is shown in Table 3.

Table 3. Azeotropic Mixtures of Carbon Tetrachloride

Second component	Boiling point of azeotrope, °C	CCl ₄ , wt %
<i>n</i> -butyl alcohol	77	97.5
acetic acid	77	97
ethyl nitrate	75	84.5
ethyl alcohol	65	84
nitromethane	71	83
ethylene dichloride	76	79
acetone	56	11.5

Many polymer films, eg, polyethylene and polyacrylonitrile, are permeable to carbon tetrachloride vapor (1). Carbon tetrachloride vapor affects the explosion limits of several gaseous mixtures, eg, air-hydrogen and air-methane. The extinctive effect that carbon tetrachloride has on a flame, mainly because of its cooling action, is derived from its high thermal capacity (2).

As chlorination proceeds from methyl chloride to carbon tetrachloride, the length of the C–Cl bond is decreased from 0.1786 nm in the former to 0.1755 nm in the latter (3). At ca 400°C, thermal decomposition of carbon tetrachloride occurs very slowly, whereas at 900–1300°C dissociation is extensive, forming perchloroethylene and hexachloroethane and liberating some chlorine. Subjecting the vapor to an electric arc also forms perchloroethylene and hexachloroethane, as well as hexachlorobenzene, elementary carbon, and chlorine.

A cold mixture of carbon tetrachloride and water, seeded with crystals of chloroform hydrate, yields crystals of a hydrate that decomposes at 1.4–1.49°C and 101.3 kPa (760 mm Hg). Carbon tetrachloride is the chloromethane least resistant to oxidative breakdown. One gram of CCl₄ mixed with air and heated to 335°C in the presence of iron produces 375 mg of phosgene. Only 2.4 mg of phosgene is produced from 1 g of chloroform under the same conditions (4). When mixed with excess water and heated to 250°C, carbon tetrachloride decomposes to carbon dioxide and hydrochloric acid; if the quantity of water is limited, phosgene is produced. This decomposition also occurs when wet carbon tetrachloride is exposed to uv irradiation (253.7 nm) at ordinary temperatures (5). Chloromethanes, hexachloroethane, and perchloroethylene are formed with steam at high temperatures. A similar decomposition occurs when carbon tetrachloride vapor is heated with some metallic oxides, eg, aluminum and magnesium oxides. An aqueous suspension of carbon tetrachloride droplets exposed to ultrasonic irradiation at ordinary temperature decomposes to carbon dioxide, chlorine, hydrogen chloride, perchloroethylene, and hexachloroethane. Dry carbon tetrachloride does not react with most commonly used construction metals, eg, iron and nickel; it reacts very slowly with copper and lead. Like the other chloromethanes, carbon tetrachloride is reactive, sometimes explosively, with aluminum and its alloys (6–8). The presence of moisture is probably a necessary requirement for the reaction with aluminum. When carbon tetrachloride is in contact with metallic sodium or potassium, or with a liquid alloy of both metals, shock may produce an explosion (9). On heating with sodium amalgam, decomposition takes place with the formation of sodium chloride and the liberation of carbon; at 400°C an analogous reaction takes place with mercury alone.

Carbon tetrachloride can be reduced to chloroform using a platinum catalyst (10) or zinc and acid. With potassium amalgam and water, carbon tetrachloride can be totally reduced to methane. It is widely employed as an initiator in the dehydrochlorination of chloroethanes at 400–600°C:



When treated with aluminum bromide at 100°C, carbon tetrachloride is converted to carbon tetrabromide [558-13-4]; reaction with calcium iodide, CaI₂, at 75°C gives carbon tetraiodide [507-25-5]. With concentrated hydroiodic acid at 130°C, iodoform [75-47-8], CHI₃, is produced. Carbon tetrachloride is unaffected by gaseous fluorine at ordinary temperatures. Replacement of its chlorine by fluorine is brought about by reaction with hydrogen fluoride at a

temperature of 230–300°C and a pressure of 5.17–6.89 MPa (750–1000 psi), producing mainly dichlorodifluoromethane (11,12). Replacement of more than two chlorine atoms in carbon tetrachloride with fluorine from hydrogen fluoride requires other techniques (13).

Carbon tetrachloride forms telomers with ethylene and certain other olefins (14–16). The mixture of liquid products derived from ethylene telomerization may be represented CCl₃(CH₂CHCl)_{*n*}Cl in which *n* is a small number. Reaction of ethylene and carbon tetrachloride takes place under pressure and is induced by the presence of a peroxygen compound, eg, benzoyl peroxide (17–19) or metal carbonyls (14,15).

Benzene reacts with carbon tetrachloride in the presence of anhydrous aluminum chloride to give triphenylchloromethane; no tetraphenylmethane is formed (20). At elevated temperatures, carbon tetrachloride attacks silica gel forming a silicon oxychloride (21).

Manufacture

For many years chlorination of carbon disulfide was the only process used to manufacture carbon tetrachloride. In the 1950s, chlorination of hydrocarbons, particularly methane, became more popular in the United States. Many hydrocarbons and chlorinated hydrocarbons are now used to feed chlorination reactors to make carbon tetrachloride.

Chlorination of Hydrocarbons or Chlorinated Hydrocarbons. Chlorination at pyrolytic temperatures is often referred to as chlorinolysis because it involves a simultaneous breakdown of the organics and chlorination of the molecular fragments. A number of processes have been described for the production of carbon tetrachloride by the chlorinolysis of various hydrocarbon or chlorinated hydrocarbon waste streams (22–24), but most literature reports the use of methane as the primary feed. The quantity of carbon tetrachloride produced depends somewhat on the nature of the hydrocarbon starting material but more on the conditions of chlorination. The principal by-product is perchloroethylene with small amounts of hexachloroethane, hexachlorobutadiene, and hexachlorobenzene. In the HbIs process, a 5:1 mixture by volume of chlorine and methane reacts at 650°C; the temperature is maintained by control of the gas flow rate. A heat exchanger cools the exit gas to 450°C, and more methane is added to the gas stream in a second reactor. The use of a fluidized-bed-type reactor is known (25,26). Carbon can be chlorinated to carbon tetrachloride in a fluidized bed (27).

Oxychlorination of Hydrocarbons. Methane was oxychlorinated with HCl and oxygen over a 4:3:3 CuCl–CuCl₂–KCl molten mixture to give a mixture of chlorinated methanes, 60 mol % of which was carbon tetrachloride (28). Aqueous 20% HCl was used in the multistep process as the source of the acid. Anhydrous HCl is more typically used. Other oxychlorination processes can be made to yield high percentages of carbon tetrachloride starting from any of several hydrocarbon feeds (29–31). The typical reaction temperature is 400–600°C (see CHLOROCARBONS AND CHLOROHYDROCARBONS, METHYL CHLORIDE; METHYLENE CHLORIDE; AND CHLOROFORM).

Carbon Disulfide Chlorination. The chlorination of carbon disulfide [75-15-0] is a very old method of producing carbon tetrachloride that is still practiced commercially in the United States. In this process CS₂ reacts continuously with chlorine in an annular reactor at 105–130°C. Product CCl₄ is separated by distillation to a CS₂ content of 0–5 ppm. By-product S₂Cl₂ is reduced in a reactor at 450°C with hydrogen without a catalyst to give sulfur of 99.985% purity (32). Other processes use ferric chloride as a catalyst (33,34).

Economic Aspects

Chlorofluorocarbon gases (CFCs), such as CFC-12 dichlorodifluoromethane [75-71-8], CCl₂F₂, and CFC-11 fluorotrichloromethane [75-69-4], CCl₃F, were introduced as aerosol propellants in the late 1950s and early 1960s. From 1960 to 1970, carbon tetrachloride, the feedstock for these compounds, averaged a growth rate of 10.7% per year (Table 4). From 1970 to 1974, as less expensive propellants became available, production of fluorocarbon propellants increased at a rate of only about 7.2%/yr even though overall aerosol consumption grew ca 10%/yr during the same period. In 1978 the use of chlorofluorocarbons in aerosols was essentially banned by the EPA. During the period 1979 to 1988 the compounded growth rate for carbon tetrachloride production was –0.7%/yr (35). This is projected to decrease to –3%/yr for the years 1989 to 1993. Production of CFC-11 and -12 is slated to be phased out by the year 2000, though it will probably decrease faster than that as replacement HCFCs become available. The U.S. producers of carbon tetrachloride and their capacities appear in Table 5. All methylene chloride and chloroform producers also make a small amount of carbon tetrachloride as a by-product. Those producers are not listed in Table 5 since the amount of carbon tetrachloride made is small and varies depending on the ratio of methylene chloride to chloroform made.

Table 4. U.S. Carbon Tetrachloride Production and Price Statistics^a

Year	Total production, 10 ³ t	Total sales, 10 ³ t	Total value, 10 ⁶ \$	Unit value, \$/kg
1960	168.8	151.3	27.14	0.18
1965	269.3	231.1	37.49	0.15
1970	458.7	381.6	44.09	0.11
1975	411.2	219.6	65.9	0.31
1976	388.6	208.2	60.3	0.29
1977	367.76	175.22	49.08	0.29
1978	335.01	165.18	41.70	0.24
1979	324.76	159.47	40.02	0.24
1980	322.54	174.70	44.13	0.24
1981	330.22	175.28	48.78	0.29
1982	267.02	141.04	39.89	0.29
1983	260.38	156.43	44.46	0.29
1984	324.11	159.65	54.47	0.35
1985	293.46	163.79	58.22	0.35
1986	284.99	225.39	68.87	0.31
1987	305.52	326.28	102.07	0.31
1988	346.08	386.03	129.43	0.33

^a Courtesy of U.S. International Trade Commission.

Table 5. U.S. Producers of Carbon Tetrachloride^a

Producer	Location	Capacity, 10 ³ t/yr
The Dow Chemical Company	Pittsburg, Calif.	36.4
The Dow Chemical Company	Plaquemine, La.	45.5
Vulcan Materials	Geismar, La.	40.9
Vulcan Materials	Wichita, Kans.	27.3
Akzo	LeMoyne, Ala.	118.2
LCP	Moundsville, W.Va.	3.6
<i>Total</i>		<i>271.9</i>

^a Ref. 35.

In 1978 there were 10 producing carbon tetrachloride plants in the United States. The number has decreased to the six listed, though the total capacity has decreased only about 10%.

List prices do not reflect actual market conditions because of overcapacity and the shrinking nature of the market. Although present U.S. carbon tetrachloride capacity of 271,900 t/yr is far in excess of demand, many installations are capable of producing other chlorinated hydrocarbons such as perchloroethylene.

Standards and Analysis

The most widely used method of analysis for carbon tetrachloride is gas chromatography. A capillary column medium that does a very good job in separating most chlorinated hydrocarbons is methyl silicone or methyl (5% phenyl) silicone. The detector of choice is a flame ionization detector. Typical molar response factors for the chlorinated methanes are methyl chloride, 2.05; methylene chloride, 2.2; chloroform, 2.8; and carbon tetrachloride, 3.1, where methane is defined as having a molar response factor of 2.00. Most two-carbon chlorinated hydrocarbons have a molar response factor of about 1.0 on the same basis.

A good technical grade of carbon tetrachloride contains not more than the following amounts of impurities: 1 ppm acidity as HCl, 1 ppm carbon disulfide if manufactured by carbon disulfide chlorination, 20 ppm bromine, 200 ppm water, and 150 ppm chloroform. The residue should not exceed 10 ppm on total evaporation. The product should give no acid reaction with bromophenol blue, and the starch iodine test should indicate the absence of free chlorine.

When heated with pyrocatechol [720-80-9], copper powder, and alcoholic sodium hydroxide, carbon tetrachloride gives a blue color that changes to red on addition of hydrochloric acid. This color reaction is not produced by chloroform. Quantitative analysis of carbon tetrachloride may be done by first decomposing the sample free of organic and inorganic chlorides, heating in a sealed tube with alcoholic potash, and subsequently determining the potassium chloride formed as the silver halide. The Zeiss interference refractometer has been used to determine the concentration of carbon tetrachloride vapor in air (36).

Health and Safety Factors

All persons who have occasion to use or handle carbon tetrachloride should be thoroughly instructed and adequately supervised in the proper methods of handling the substance to prevent or minimize exposure to the liquid or its vapors and in the proper methods of disposing of this chemical.

Carbon tetrachloride is the oldest and was the most extensively used chlorinated solvent in degreasing and dry-cleaning operations for many years. Consequently, its narcotic and toxic properties have been the subject of much investigation. Careful investigations have repeatedly shown carbon tetrachloride to be one of the most harmful of the common solvents (37).

Carbon tetrachloride is toxic by inhalation of its vapor and oral intake of the liquid. Inhalation of the vapor constitutes the principal hazard. Exposure to excessive levels of vapor is characterized by two types of response: an anesthetic effect similar to that caused by compounds such as diethyl ether and chloroform; and organic injury to the tissues of certain organs, in particular the liver and kidneys. This type of injury may not become evident until 1–10 days after exposure. The nature of the effect is determined largely by the vapor concentration but the extent or severity of the effect is determined principally by the duration of exposure (38).

Organic injury may result from single prolonged exposure to carbon tetrachloride vapor or from repeated short duration exposures. Serious and fatal injuries are usually the result of a single prolonged exposure. Vapor concentrations of only a few hundred parts per million may be sufficient to cause injury. Symptoms of exposure include nausea and vomiting, headache, burning of eyes and/or throat, drowsiness, abdominal pain or discomfort, weakness, and muscle stiffness and soreness. Prolonged or repeated exposure to carbon tetrachloride vapor or liquid may result in subacute or chronic poisoning. Consequently, a threshold limit value of 5 ppm by volume of carbon tetrachloride in air has been established by ACGIH as a maximum safe concentration for daily eight-hour exposure. The OSHA permissible exposure level is 2 ppm.

Occasional brief contacts of liquid carbon tetrachloride with unbroken skin do not produce irritation, though the skin may feel dry because of removal of natural oils. Prolonged and repeated contacts may cause dermatitis, cracking of the skin, and danger of secondary infection. Carbon tetrachloride is apparently absorbed through the skin but at such a slow rate that there is no significant hazard of systemic poisoning in normal industrial operations.

In most situations, adequate, usually forced, ventilation is necessary to prevent excessive exposure. Persons who drink alcohol excessively or have liver, kidney, or heart diseases should be excluded from any exposure to carbon tetrachloride. All individuals regularly exposed to carbon tetrachloride should receive periodic examinations by a physician acquainted with the occupational hazard involved. These examinations should include special attention to the kidneys and the liver. There is no known specific antidote for carbon tetrachloride poisoning. Treatment is symptomatic and supportive. Alcohol, oils, fats, and epinephrine should not be given to any person who has been exposed to carbon tetrachloride. Following exposure, the individual should be kept under observation long enough to permit the physician to determine whether liver or kidney injury has occurred. Artificial dialysis may be necessary in cases of severe renal failure.

Handling and Storage

Although in the dry state carbon tetrachloride may be stored indefinitely in contact with some metal surfaces, its decomposition upon contact with water or on heating in air makes it desirable, if not always necessary, to add a small quantity of stabilizer to the commercial product. A number of compounds have been claimed to be effective stabilizers for carbon tetrachloride, eg, alkyl cyanamides such as diethyl cyanamide (39), 0.34–1% diphenylamine (40), ethyl acetate to protect copper (41), up to 1% ethyl cyanide (42), fatty acid derivatives to protect aluminum (43), hexamethylenetetramine (44), resins and amines (45), thiocarbamide (46), and a ureide, ie, guanidine (47).

Small quantities of carbon tetrachloride can be shipped in 1, 5, and 55 gallon (208 L) metal containers. Larger quantities are shipped by tank truck, tank car, barge, and ship. Seamless stainless steel, Teflon, or seamless bronze hose is recommended with asbestos, Teflon, Viton, or neoprene gaskets. Special precautions should be taken to prevent contact with aluminum, magnesium metal, and their alloys (48).

Uses

Carbon tetrachloride was formerly used for metal degreasing, dry-cleaning fluid, fabric spotting fluid, fire extinguisher fluid, grain fumigant, and reaction medium. However, as its toxicity became recognized, it was replaced by less toxic chlorinated hydrocarbons in metal and fabric cleaning applications. During the 1950s the demand for carbon tetrachloride as a raw material in the manufacture of chlorofluorocarbons increased and the net result was continued growth for the product. In 1970, carbon tetrachloride was banned from all use in consumer goods in the United States. Its current principal applications include chlorofluorocarbon production (CFC-11 and -12) and some small use as a reaction medium or chemical intermediate. Chlorofluorocarbons 11 and 12, trichloromonofluoromethane [75-69-4], and dichlorodifluoromethane [75-71-8], respectively, are made by the catalytic reaction of hydrogen fluoride with carbon tetrachloride. These products will decline significantly long term as the Montreal Protocol takes effect.

Regulation

Carbon tetrachloride, as are the other chlorinated methanes, is heavily regulated at the national, state, and local level. The manufacturing, storage, and

disposal of carbon tetrachloride may be regulated. Carbon tetrachloride is reportable under SARA 312 (inventory) and 313 (emissions). In addition, the nonpermitted release of carbon tetrachloride is reportable at a 10 pound (4.5 kg) quantity under CERCLA. Finally, fugitive monitoring regulations and programs may apply to individual facilities. The discharge of carbon tetrachloride to the waterways may be regulated under OCPSF guidelines or other permitted parameters. Disposal of carbon tetrachloride and carbon tetrachloride-containing wastes may be regulated under RCRA as a discarded commercial chemical (U0211), a nonspecific source waste (F001), or as an extractable at 0.5 mg/L under the TCLP (D019). The potential exposure to carbon tetrachloride by workers may be regulated by OSHA or the state Industrial Hygiene Department. In addition, various state and local regulations may impose other reporting and regulatory standards. Contacting the Environmental or Regulatory Compliance Department before importing, purchasing, selling, using, or disposing of carbon tetrachloride is highly recommended.

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